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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549**

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**FORM S-1  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

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**MeiraGTx Holdings plc**

(Exact name of registrant as specified in its charter)

**Cayman Islands**  
(State or other jurisdiction of  
incorporation or organization)

**2836**  
(Primary Standard Industrial  
Classification Code Number)

**Not applicable**  
(I.R.S. Employer  
Identification No.)

**430 East 29th Street, 10th Floor  
New York, NY 10016  
(646) 490-2965**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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**Alexandria Forbes, Ph.D.  
MeiraGTx LLC  
430 East 29th Street, 10th Floor  
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(646) 490-2965**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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**Approximate date of commencement of proposed sale to the public:  
As soon as practicable after this Registration Statement is declared effective.**

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company” and “emerging growth company” in Rule 12b-2 of the Exchange Act.

<b>Large accelerated filer</b>	<input type="checkbox"/>	<b>Accelerated filer</b>	<input type="checkbox"/>
<b>Non-accelerated filer</b>	<input checked="" type="checkbox"/>	<b>Smaller reporting company</b>	<input type="checkbox"/>
<b>(Do not check if a smaller reporting company)</b>		<b>Emerging growth company</b>	<input checked="" type="checkbox"/>

If an emerging growth company, indicate by checkmark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided to Section 7(a)(2)(B) of the Securities Act.

**CALCULATION OF REGISTRATION FEE**

Title of Each Class of Securities To Be Registered	Proposed Maximum Aggregate Offering Price(1)(2)	Amount of Registration Fee(3)
Ordinary shares, \$0.00001 nominal value per share	\$86,250,000	\$10,738.13

- (1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.  
(2) Includes the aggregate offering price of additional shares that the underwriters have the option to purchase.  
(3) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.**

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion  
Preliminary Prospectus dated May 14, 2018.

**PROSPECTUS**

**Shares**



**Ordinary Shares**

This is MeiraGTx Holdings plc's initial public offering. We are offering \_\_\_\_\_ of our ordinary shares.

We expect the initial public offering price to be between \$ \_\_\_\_\_ and \$ \_\_\_\_\_ per ordinary share. Currently, no public market exists for our ordinary shares. After pricing of the offering, we expect that our ordinary shares will trade on the Nasdaq Global Market under the symbol "MGTX."

We are an "emerging growth company" under the federal securities laws and are subject to reduced public company disclosure standards. See "Prospectus Summary—Implications of Being an Emerging Growth Company."

Investing in our ordinary shares involves risks that are described in the "[Risk Factors](#)" section beginning on page 12 of this prospectus.

	<u>Per Share</u>	<u>Total</u>
Public offering price	\$ _____	\$ _____
Underwriting discount(1)	\$ _____	\$ _____
Proceeds, before expenses, to us	\$ _____	\$ _____

(1) We refer you to "Underwriting" beginning on page 187 for additional information regarding underwriting compensation.

The underwriters may also exercise their option to purchase up to an additional \_\_\_\_\_ ordinary shares from us, at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The ordinary shares will be ready for delivery on or about \_\_\_\_\_, 2018.

*Joint Book-Running Managers*

**BofA Merrill Lynch**

**Barclays**

**Evercore ISI**

*Lead Manager*

**Chardan**

The date of this prospectus is \_\_\_\_\_, 2018.

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Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of our ordinary shares. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the ordinary shares and the distribution of this prospectus outside the United States.

## ABOUT THIS PROSPECTUS

Prior to the completion of this offering, we will undertake a corporate reorganization, pursuant to which MeiraGTx Limited will become a wholly owned subsidiary of MeiraGTx Holdings plc, an exempted company incorporated under the laws of the Cayman Islands with nominal assets and liabilities, which will not have conducted any operations prior to this offering other than acquiring the entire issued share capital of MeiraGTx Limited and other actions incidental to such acquisition and its incorporation. MeiraGTx Holdings plc will be the issuer of ordinary shares in this offering. Following the corporate reorganization, our financial statements will present the results of operations of MeiraGTx Holdings plc and its consolidated subsidiaries.

Unless otherwise indicated or the context otherwise requires, all references in this prospectus to the terms “MeiraGTx,” the “Company,” “we,” “us” and “our” refer to MeiraGTx Limited and its wholly owned subsidiaries prior to the completion of our corporate reorganization and MeiraGTx Holdings plc and its subsidiaries after the completion of our corporate reorganization.

We have proprietary rights to trademarks, trade names and service marks appearing in this prospectus that are important to our business. Solely for convenience, the trademarks, trade names and service marks may appear in this prospectus without the ® and TM symbols, but any such references are not intended to indicate, in any way, that we forgo or will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, trade names and service marks. All trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

## PROSPECTUS SUMMARY

*This summary highlights, and is qualified in its entirety by, the more detailed information and financial statements included elsewhere in this prospectus. This summary does not contain all of the information that may be important to you in making your investment decision. You should read this entire prospectus carefully, especially the “Risk Factors” section beginning on page 12 and our consolidated financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our ordinary shares.*

### Overview

We are a vertically integrated, clinical stage gene therapy company with four ongoing clinical programs and a broad pipeline of preclinical and research programs. We have core capabilities in viral vector design and optimization and gene therapy manufacturing, as well as a potentially transformative gene regulation technology. Led by an experienced management team, we have taken a portfolio approach by licensing, acquiring and developing technologies that give us depth across both product candidates and indications. Though initially focusing on the eye, salivary gland and central nervous system, we intend to expand our focus in the future to develop additional gene therapy treatments for patients suffering from a range of serious diseases.

We operate a flexible and scalable viral vector manufacturing facility that we expect can supply our current clinical and preclinical programs through regulatory approval and, should they be approved, provide sufficient capacity for commercial production. Completed in early 2018 and designed to meet global regulatory requirements, including the current good manufacturing practices, or cGMP, required by the U.S. Food and Drug Administration, or FDA, our 29,000 square foot facility has two cell production suites, three independent viral vector production suites providing multi-product and multi-viral vector manufacturing capabilities and an integrated, flexible fill-and-finish suite.

We have also established a comprehensive platform for the efficient clinical development of the next generation of gene therapies and manufacturing in accordance with cGMP. Our deep understanding of disease models informs our development of potency assays for the cGMP production of our product candidates, and our teams experienced in viral vector design work closely with our process development team to design viral vectors and develop proprietary production cell lines for efficient scaling of manufacturing processes.

We are also developing a potentially transformative technology to enable the use of small molecules to turn gene therapy product candidates on and off. The aim of this gene regulation platform is to convert gene therapy into a generalizable delivery mechanism for biologic drugs using a small molecule “switch” for temporal control. We believe the capacity for temporal control of gene therapy products has the potential to transform the gene therapy landscape by opening up new treatment possibilities.

### Our Pipeline

Our initial focus is on three distinct areas of unmet medical need: inherited retinal diseases, or IRDs, severe forms of xerostomia and neurodegenerative diseases. Utilizing our product development platform, we have assembled a pipeline of gene therapies to treat these serious diseases. Our criteria for selecting our initial product candidates included:

- unmet medical need;
- high potential for meaningful clinical benefit;
- promising preclinical data using multiple animal models as well as human stem cell derived organoids;

- compartmentalized anatomy of target tissue and the partially immune protected nature of target tissue; and
- understanding of the disease state from natural history studies and detailed long-term characterization of patients prior to entry into gene therapy treatment studies.

A summary of our product candidates is below. We retain worldwide development and commercialization rights to all of our product candidates.

Product Candidate	Indication	Development Stage			Status
		Preclinical	Phase 1/2	Phase 3	
<b>Ophthalmology Programs</b>					
AAV-CNGB3	<b>Achromatopsia</b> ( <i>CNGB3</i> )	Orphan U.S. & EU; RPDD; PRIME <sup>(1,2,4)</sup>			• Phase 1/2 ongoing in UK <sup>(5)</sup>
AAV-CNGA3	<b>Achromatopsia</b> ( <i>CNGA3</i> )				• Phase 1/2 expected initiation in 2019
AAV-RPGR	<b>X-linked RP</b> ( <i>RPGR</i> )	Orphan U.S. & EU; Fast Track Designation <sup>(1,2,6)</sup>			• Phase 1/2 ongoing
AAV-RPE65	<b>RPE65-Deficiency</b> ( <i>RPE65</i> )	Orphan U.S. & EU; RPDD <sup>(1,2,6)</sup>			• Phase 1/2 ongoing
AAV-AIPL1	<b>LCA4</b> ( <i>AIPL1</i> )	<b>Compassionate Use</b> Orphan U.S. & EU <sup>(1,2)</sup>			• UK Specials License <sup>(7)</sup> approved October 2017
A006	<b>Wet AMD</b> ( <i>anti-VEGFR2</i> )				• First in man clinical trials expected 2019
<b>Salivary Gland Programs</b>					
AAV-AQP1	<b>Xerostomia</b> ( <i>hAQP1</i> )	Orphan U.S. <sup>(1)</sup>			• Phase 1 ongoing
AAV-AQP1	<b>Sjogren's</b> ( <i>hAQP1</i> )				• Phase 1/2 expected initiation in 2019
<b>Neurodegenerative Diseases Program</b>					
AAV-UPF1	<b>ALS</b> ( <i>UPF1</i> )				• First in man clinical trials expected 2019

1. Orphan drug designation by the FDA.
2. Orphan drug designation by European Medicines Agency, or the EMA.
3. Rare pediatric disease designation by Offices of Orphan Products Development and Pediatric Therapeutics of the FDA.
4. Priority medicines, or PRIME, designation by the EMA.
5. The IND for AAV-CNGB3 has not been opened yet because the FDA had a question about our device compatibility assay, placing the IND on clinical hold until the question has been satisfactorily answered.
6. Fast Track designation by the FDA.
7. Manufactured under a specials license and released for compassionate use in the United Kingdom, or UK.

In addition to these clinical and preclinical programs, we have preclinical and research programs in other indications and novel molecular technologies that we aim to advance into clinical development, including:

- neovascular age related macular degeneration, or wet AMD – use of a gene therapy product to deliver an antibody targeting the vascular endothelial growth factor receptor 2, or anti-VEGFR2, with the aim of blocking disease related vascular formation in the eye;
- geographic atrophy age related macular degeneration, or dry AMD – use of gene therapy technology to introduce light sensitive molecules into rod photoreceptors in order to restore some aspects of vision lost in this disease;
- amyotrophic lateral sclerosis, or ALS – targeting dysregulation of neuronal RNA processing, which we believe may lead to the degeneration of motor neurons that occurs in ALS;
- Alzheimer’s disease – targeting endosomal trafficking, which is a central mechanism that we believe underlies Alzheimer’s disease; and
- gene regulation – use of our proprietary RNA shape regulation cassette to switch gene therapy product candidates on and off with small molecules, potentially transforming gene therapy technology into a delivery mechanism for a broad array of biologic drugs.

### **Our Ophthalmology Programs**

Eye diseases are our first area of clinical focus and we aim to provide treatments with durable, long-term clinical benefit that will halt vision loss in patients. We currently have three ongoing clinical programs in IRDs with an additional program expected to initiate a Phase 1/2 clinical trial in 2019. The targets of our three ongoing Phase 1/2 ophthalmology programs include achromatopsia related to mutations in *CNGB3*, X-linked retinitis pigmentosa related to mutations in *RPGR*, and inherited retinal dystrophy caused by mutations in *RPE65*. We also have a product candidate that was manufactured and released for compassionate use under a special license in the United Kingdom to treat patients with Leber congenital amaurosis 4, or *LCA4*, caused by mutations in *AIPL1*. For each of our Phase 1/2 clinical programs we also have a prospectively designed natural history study ongoing, which includes the same endpoints as our corresponding gene therapy treatment trial. We believe use of these natural history studies differentiates our programs by providing patient populations to facilitate the efficient execution of our clinical trials and offering insight into the appropriate endpoints for regulatory approval of our gene therapy product candidates. In addition to these clinical programs, we have preclinical programs that apply novel approaches to both wet and dry AMD.

The FDA and EMA have granted orphan drug designation to each product candidate in our ongoing clinical programs, including those treating mutations in *CNGB3*, *RPGR* and *RPE65*, as well as our product candidate to treat mutations in *AIPL1*. The FDA also granted rare pediatric disease designation for our clinical programs treating mutations in *RPE65* and *CNGB3* and Fast Track designation to our clinical program treating XLRP caused by mutations in *RPGR*. We have also received PRIME designation from the EMA for our clinical program treating mutations in *CNGB3*.

The deep scientific and clinical understanding of IRDs driving our approach to gene therapy development helps us to optimize our product candidates for each specific genetic mutation and phenotype. We develop our viral vectors by selecting and modifying proprietary cell specific promoters, selecting appropriate capsids for transfection of target cells and refining the vector for efficient production and scalable manufacturing. Not only does this allow us to synergistically target a portfolio of inherited eye conditions, we also believe it has potential to be applied to the development of gene-based therapies for other diseases.

Our longstanding relationships with leading institutions in retinal disease treatment, including Moorfields Eye Hospital in London, the University of Michigan Kellogg Eye Center, Massachusetts Eye and Ear,



the Medical College of Wisconsin & Froedtert Hospital and the Casey Eye Institute at the Oregon Health & Science University, provide us with access to experts whose guidance and insight informs our development strategy, as well potential patients for our clinical trials.

### **Our Salivary Gland Programs**

Our second area of clinical focus is xerostomia, a chronic and debilitating disorder of the salivary glands in which saliva production is impaired. Xerostomia may be caused by a number of different insults to the salivary glands, including radiation therapy for head and neck cancer and certain autoimmune diseases. A Phase 1 clinical trial of our gene therapy product candidate, AAV-AQP1, is ongoing in patients who have survived cancer free for five or more years following treatment for head and neck cancer and are suffering from grade 2 or 3 radiation induced late xerostomia, or RIX. There are approximately 170,000 grade 2 or 3 RIX patients who have survived two or more years after radiation treatment for head and neck cancer in the United States, with approximately 10,000 new cases each year. We also intend to initiate a Phase 1/2 clinical trial of AAV-AQP1 for the treatment of patients with chronic xerostomia caused by Sjogren's syndrome, an autoimmune disease affecting more than two million people in the United States.

The FDA has granted orphan drug designation to AAV-AQP1.

### **Our Neurodegenerative Disease Programs**

Neurodegenerative diseases are our third area of focus. Our first target indication is ALS and we expect to file an investigational new drug application, or IND, and initiate a clinical trial of our first product candidate for the treatment of ALS in 2019. We believe our approach to treating ALS patients is differentiated because, rather than targeting a specific genetic defect that defines a small subset of ALS patients, we aim to target the underlying cell biology driving motor neuron death in ALS, potentially enabling us to treat a broader patient population that includes both sporadic and inherited forms of the disease. Increasing evidence suggests a critical role of RNA metabolism in neuronal cells, in particular in motor neurons that are specifically affected in ALS. We believe that dysregulation of neuronal RNA processes results in the degeneration of motor neuron that leads to ALS. Using our viral vector product candidate, AAV-UPF1, we target the central quality control system regulating RNA in motor neurons with the aim of enhancing motor neuron survival in ALS patients.

We have an Alzheimer's disease program that is likewise directed towards the underlying cell biology of the disease, in this case endosomal trafficking, a mechanism cells use to cycle proteins to the cell surface. Over the past decade, evidence has emerged supporting endosomal trafficking dysfunction in neurons as a central process in the early etiology of Alzheimer's disease. In particular, a master regulator of trafficking out of the endosomes called retromer has been implicated. We are in the process of identifying the optimal approach to restoring normal endosomal function to the neurons that are the first to be affected in Alzheimer's disease and appear to drive the initiation of the disease. In parallel, we are developing and validating biomarkers of endosomal dysfunction and pre-symptomatic Alzheimer's disease. We believe this approach may also provide a framework for treating certain forms of Parkinson's disease that are also associated with endosomal dysfunction.

### **Our Strengths**

In addition to our four ongoing clinical programs, we have a broad pipeline of preclinical programs, core capabilities in viral vector design and optimization, gene therapy manufacturing and a potentially transformative gene regulation technology. Utilizing the following key strengths, we aim to develop, commercialize and expand our portfolio of gene therapy product candidates.

- **Deep Expertise in Gene Therapy Development:** Our expertise in viral vector design, optimization and process development allows us to efficiently advance gene therapy product candidates from preclinical development to cGMP manufacturing and human clinical development through commercialization.

- **Potentially Transformative Gene Regulation Technology Platform:** We are developing proprietary technology for innovative gene therapy treatments whose expression can be turned on and off with an easily administered small molecule. We believe the capacity for temporal control of gene therapy products has the potential to transform the gene therapy landscape by opening up new treatment possibilities.
- **Manufacturing Capabilities and Capacity:** We have a flexible and scalable cGMP manufacturing facility and production process, which we expect can supply all of our current clinical and preclinical programs through regulatory approval and, should they be approved, provide sufficient capacity for their commercial production.
- **Robust and Diverse Clinical and Preclinical Pipeline:** Applying our portfolio approach to gene therapy product development, our initial focus is on treatments for IRDs, salivary glands disorders and neurodegenerative diseases with potential for accelerated approval and has produced four ongoing clinical programs and multiple preclinical development programs.
- **Relationships with Leading Institutions:** Our longstanding relationships with leading institutions and experts provides us with guidance on development strategy and access to potential patients for our clinical trials.
- **Natural History Study Data:** We sponsor ongoing prospective long-term natural history studies in IRDs that facilitate our ability to efficiently enroll our treatment studies, potentially reducing clinical trial timelines and providing insight into the appropriate endpoints for regulatory approval.

### **Our Strategy**

Our goal is to develop and commercialize innovative gene therapy products to treat serious disorders and broaden the scope of indications that may be treatable by our gene therapies. Our strategy to achieve this goal is to:

- successfully complete clinical development, obtain regulatory approval and commercialize our pipeline of gene therapy product candidates to treat disorders of the eye and salivary gland;
- continue to advance the development of our pipeline of gene therapy product candidates for the treatment of neurodegenerative disorders;
- utilize our viral vector design and optimization capabilities to identify and develop new gene therapies for other serious diseases;
- advance the development of our potentially transformative proprietary technology for regulating the activity of gene therapy products using small molecules and initiate clinical trials of new product candidates; and
- evaluate strategic collaborations with other biotechnology and pharmaceutical companies to leverage our capabilities, manufacturing capacity and proprietary gene regulation technology.

### **Risk Factors**

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled “Risk Factors” immediately following this prospectus summary. Some of these risks are:

- We have incurred significant losses since inception and anticipate that we will incur continued losses for the foreseeable future, and may never achieve or maintain profitability.

- We will require additional capital to fund our operations, which may not be available on acceptable terms, if at all.
- We are heavily dependent on the success of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, our most advanced product candidates, which are still in development, and if none of them receive regulatory approval or are successfully commercialized, our business may be harmed.
- We intend to identify and develop product candidates based on our novel gene therapy platform, which makes it difficult to predict the time and cost of product candidate development. Very few products that utilize transduction technology have been approved in the United States or in Europe, and there have only been a limited number of human clinical trials involving gene therapy product candidates.
- Because gene therapy is novel and the regulatory landscape that governs any product candidates we may develop is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.
- Clinical trials are expensive, time-consuming, difficult to design and implement, and involve an uncertain outcome. Further, we may encounter substantial delays in our clinical trials.
- The affected populations for our other product candidates may be smaller than we or third parties currently project, which may affect the addressable markets for our product candidates.
- We and our contract manufacturer for plasmid are subject to significant regulation with respect to manufacturing our products. Our manufacturing facilities and the third-party manufacturing facility which we rely on may not continue to meet regulatory requirements and have limited capacity.
- We depend on proprietary technology licensed from others. If we lose our existing licenses or are unable to acquire or license additional proprietary rights from third parties, we may not be able to continue developing our product candidates. In addition, if we are unable to obtain and maintain patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.
- We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.

#### **Implications of Being an Emerging Growth Company**

As a company with less than \$1.07 billion in revenue during our last fiscal year, we qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or JOBS Act. An “emerging growth company” may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements and only two years of related Management’s Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We may take advantage of these provisions until the last day of 2023. However, if certain events occur prior to the end of 2023, including if we become a “large accelerated filer,” our annual gross revenue exceeds \$1.07 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of 2023.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our shareholders may be different than you might receive from other public reporting companies in which you hold equity interests.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have elected to take advantage of this extended transition period.

### **Corporate Information**

MeiraGTx Limited, which will be a subsidiary of MeiraGTx Holdings plc and its predecessor accounting entity upon closing of the offering was formed as a private limited company under the laws of England and Wales and began operations on March 20, 2015, with the company number 09501998. Our registered office address is at 92 Britannia Walk, London N1 7NQ, England. Our principal executive offices are located at 430 East 29<sup>th</sup> Street, 10<sup>th</sup> Floor, New York, New York 10016 and our telephone number is (646) 490-2965. Our website address is [www.meiragtx.com](http://www.meiragtx.com). The information contained in, or accessible through, our website does not constitute a part of this prospectus.

### **Corporate Reorganization**

Prior to the completion of this offering, we will effect a reorganization. MeiraGTx Holdings plc, an exempted company incorporated under Cayman Islands law, will become the direct parent of MeiraGTx Limited and the holding company of the business and will be the issuer of ordinary shares in this offering. Prior to this offering, MeiraGTx Holdings plc will have only engaged in activities incidental to its formation, the corporate reorganization and this offering. Accordingly, financial information for MeiraGTx Holdings plc and a discussion and analysis of its results of operations and financial condition for the period of its operations prior to the reorganization would not be meaningful and are not presented. Following the corporate reorganization, our financial statements will present the results of operations of MeiraGTx Holdings plc and its consolidated subsidiaries.

**The Offering**

Ordinary shares offered by us	ordinary shares.
Ordinary shares to be outstanding after this offering	ordinary shares (or shares if the underwriters exercise their option to purchase additional ordinary shares in full).
Option to purchase additional shares	The underwriters have a 30-day option to purchase up to additional ordinary shares at the public offering price less estimated underwriting discounts and commissions.
Use of proceeds	We estimate that the net proceeds from this offering will be approximately \$ million (or approximately \$ million if the underwriters exercise their option to purchase additional ordinary shares in full), based on an assumed initial public offering price of \$ per ordinary share, after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us. We anticipate that we will use the net proceeds of this offering to continue to develop our most advanced product candidates, AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, scale-up our manufacturing facility and related processes, fund research and development of other pipeline product candidates and technologies, and pursue additional research and development efforts as set forth under “Use of Proceeds” beginning on page 71 for additional information.
Risk factors	You should carefully read the “Risk Factors” beginning on page 12 and the other information included in this prospectus for a discussion of factors you should consider carefully before deciding to invest in our ordinary shares.
Proposed Nasdaq Global Market symbol	“MGTX”
The number of our ordinary shares to be outstanding after this offering is based on including unvested restricted shares subject to repurchase, and excluding:	ordinary shares outstanding as of ,
	<ul style="list-style-type: none"><li>• 6,265,500 ordinary shares issuable upon exercise of share options outstanding under our 2016 Equity Incentive Plan, referred to as our 2016 Plan, as of March 31, 2018, at a weighted-average exercise price of \$1.37 per ordinary share; and</li><li>• additional ordinary shares reserved for future issuance under our 2018 Incentive Award Plan, referred to as our 2018 Plan, which will become effective in connection with this offering, as well as any automatic increases in the number of our ordinary shares reserved for future issuance under our 2018 Plan.</li></ul>

Unless otherwise indicated, this prospectus reflects and assumes the following:

- the consummation of our corporate reorganization prior to the closing of this offering;
- no exercise of outstanding options after March 31, 2018; and
- no exercise by the underwriters of their option to purchase additional ordinary shares.

### Summary Consolidated Financial Data

The following tables set forth our summary consolidated financial data for the period indicated. We have derived the consolidated statement of operations and comprehensive loss data for the years ended December 31, 2016 and 2017 from our audited consolidated financial statements included elsewhere in this prospectus. We have derived the consolidated balance sheet data as of March 31, 2018 and the consolidated statement of operations and comprehensive loss data for the three months ended March 31, 2017 and 2018 from our unaudited financial statements included elsewhere in this prospectus. These unaudited financial statements have been prepared on a basis consistent with our audited financial statements and, in our opinion, contain all adjustments, consisting of normal and recurring adjustments, necessary for the fair presentation of such financial data. Our historical results are not necessarily indicative of the results that should be expected for any future period. You should read the following summary consolidated financial data together with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and the related notes included elsewhere in this prospectus.

	<u>Year Ended December 31,</u>		<u>Three Months Ended March 31,</u>	
	<u>2016</u>	<u>2017</u>	<u>2017</u>	<u>2018</u>
<b>Consolidated Statement of Operations and Comprehensive Loss Data:</b>				
Operating expenses:				
General and administrative	\$ 6,026,529	\$ 9,325,017	\$ 2,148,540	\$ 11,122,016
Research and development	14,037,918	22,359,712	4,823,357	6,927,322
Total operating expenses	<u>20,064,447</u>	<u>31,684,729</u>	<u>6,971,897</u>	<u>18,049,338</u>
Loss from operations	(20,064,447)	(31,684,729)	(6,971,897)	(18,049,338)
Other non-operating income (expense):				
Foreign currency gain	265,543	1,676,117	149,249	978,624
Convertible note inducement expense	—	(553,500)	—	—
Change in fair value of warrant liability	—	(465,633)	—	669,408
Interest income	32,068	26,073	10,389	25,308
Interest expense	(25,440)	(42,863)	(8,126)	(27,355)
Net loss	(19,792,276)	(31,044,535)	(6,820,385)	(16,403,353)
Net loss attributable to non-controlling interest in subsidiary	305,883	—	—	—
Net loss attributable to MeiraGTx shareholders	(19,486,393)	(31,044,535)	(6,820,385)	(16,403,353)
Other comprehensive loss	(671,391)	(1,361,365)	(130,895)	(757,765)
Comprehensive loss	(20,157,784)	(32,405,900)	(6,951,280)	(17,161,118)
Less: comprehensive loss (income) attributable to non-controlling interest	8,520	—	—	—
Comprehensive loss attributable to MeiraGTx shareholders	<u>\$(20,149,264)</u>	<u>\$(32,405,900)</u>	<u>\$(6,951,280)</u>	<u>\$(17,161,118)</u>
Net loss attributable to MeiraGTx shareholders	\$(19,486,393)	\$(31,044,535)	\$(6,820,385)	\$(16,403,353)
Accretion on Series C preferred shares	(85,425)	(806,963)	(22,761)	(664,718)
Adjusted net loss attributable to MeiraGTx ordinary shareholders	<u>\$(19,571,818)</u>	<u>\$(31,851,498)</u>	<u>\$(6,843,146)</u>	<u>\$(17,068,071)</u>

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	Year Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
Basic and diluted net loss per ordinary share attributable to ordinary shareholders(1)	\$ (0.63)	\$ (0.96)	\$ (0.21)	\$ (0.49)
Weighted-average number of ordinary shares outstanding—basic and diluted(1)	31,098,591	33,269,157	32,851,408	34,647,368

(1) See Note 12 to our consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical basic and diluted net loss per ordinary share and the weighted-average number of shares used in the computation of the per share amounts.

	As of March 31, 2018		
	Actual	Pro Forma(1)	Pro Forma As Adjusted(2)(3)
<b>Consolidated Balance Sheet Data:</b>			
Cash and cash equivalents	\$ 32,356,851	\$	\$
Total assets	\$ 50,780,903		
Total liabilities	\$ 14,345,189		
Convertible preferred C shares	\$ 97,351,080		
Total shareholders' (deficit) equity	\$(60,915,366)		

(1) The pro forma data above gives effect to the corporate reorganization described under "Summary—Corporate Reorganization."

(2) The pro forma as adjusted data above reflects the pro forma adjustments described in footnote (1) above and the issuance and sale of ordinary shares in this offering at an assumed initial public offering price of \$ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(3) The pro forma as adjusted information discussed above is illustrative only and will depend on the actual initial public offering price and other terms of our initial public offering determined at pricing. Each \$1.00 increase (decrease) in the assumed initial public offering price of \$ per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, total assets and total shareholders' equity by \$ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million in the number of ordinary shares offered by us at the assumed initial public offering price would increase (decrease) each of cash and cash equivalents, total assets and total shareholders' equity by \$ million, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us.



## RISK FACTORS

*You should carefully consider the risks and uncertainties described below and the other information in this prospectus before making an investment in our ordinary shares. Our business, financial condition, results of operations or prospects could be adversely affected if any of these risks occurs, and as a result, the market price of our ordinary shares could decline and you could lose all or part of your investment. This prospectus also contains forward-looking statements that involve risks and uncertainties. See “Cautionary Statement Regarding Forward-Looking Statements.” Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including those set forth below.*

### **Risks Related to Our Financial Position and Need for Additional Capital**

***We have incurred significant losses since inception and anticipate that we will incur continued losses for the foreseeable future, and may never achieve or maintain profitability.***

We are a clinical stage company with limited operating history. We were formed and began operations in 2015 through the acquisition of Athena Vision Ltd. and certain assets from Kadmon Corporation, LLC. We have never been profitable and do not expect to be profitable in the foreseeable future. We have incurred net losses since inception, including net losses of approximately \$16.4 and \$6.8 million for the three months ended March 31, 2018 and 2017, respectively, and approximately \$31.0 million and \$19.8 million for the years ended December 31, 2017 and December 31, 2016, respectively. As of March 31, 2018, we had an accumulated deficit of approximately \$81.8 million. Since our inception, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facility and developing manufacturing processes, advancing the product candidates in our ophthalmology, salivary gland and neurodegenerative disease programs, building our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, and providing general and administrative support for these operations. We have not yet demonstrated an ability to successfully complete a clinical program, including large-scale, pivotal clinical trials, obtain marketing approval, manufacture product at a commercial scale, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Typically, it takes about six to ten years to develop a new drug from the time it enters Phase 1 clinical trials to when it is approved for treating patients, but in many cases it may take longer. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing genetic medicine products.

We expect to continue to incur significant expenses and additional operating losses for the foreseeable future as we seek to advance product candidates through preclinical and clinical development, expand our research and development activities, develop new product candidates, complete clinical trials, seek regulatory approval and, if we receive regulatory approval, commercialize our products. Furthermore, the costs of advancing product candidates into each succeeding clinical phase tend to increase substantially over time. The total costs to advance any of our product candidates to marketing approval in even a single jurisdiction would be substantial. Because of the numerous risks and uncertainties associated with gene therapy product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of products or achieve or maintain profitability. Our expenses will also increase substantially if and as we operate as a public company and add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our transition to a public reporting company.

Before we generate any revenue from product sales, each of our programs and product candidates will require additional preclinical and/or clinical development, potential regulatory approval in multiple jurisdictions, manufacturing, building of a commercial organization, substantial investment and significant marketing efforts. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or FDA, European Medicines Agency, or EMA, or other regulatory authorities to perform preclinical studies and

clinical trials in addition to those that we currently anticipate. These risks are further described under “—Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval” and “—Risks Related to Commercialization.” As a result, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our shareholders’ equity and working capital.

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance. If we are unable to develop and commercialize one or more of our product candidates either alone or with collaborators, or if revenues from any product candidate that receives marketing approval are insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability. If we are unable to achieve and then maintain profitability, the value of our equity securities will be adversely affected.

***We will require additional capital to fund our operations, which may not be available on acceptable terms, if at all.***

We expect to spend substantial amounts to complete the development of, seek regulatory approvals for and commercialize our product candidates. We will require additional capital beyond the proceeds of this offering, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable us to complete the development and potential commercialization of our product candidates. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our product candidate development efforts. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate certain of our research and development programs.

Our operations have consumed significant amounts of cash since inception. As of March 31, 2018, our cash and cash equivalents were \$32.4 million. Based upon our current operating plan, we believe that the net proceeds from this offering will enable us to fund our operating expenses and capital expenditure requirements for at least the next months. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the progress, timing, costs and results of our ongoing clinical development for our *CNGB3* gene therapy product candidate, AAV-CNGB3, for our *RPE65*-deficiency product candidate, AAV-RPE65, for our X-linked retinitis pigmentosa product candidate, AAV-RPGR, for our radiation induced xerostomia product candidate, AAV-AQP1, and continue to conduct our ongoing natural history studies for inherited retinal diseases, or IRDs;
- the initiation of Phase 1/2 clinical trials for our *CNGA3* gene therapy product candidate, AAV-CNGA3, and for our product candidate for the treatment of xerostomia associated with Sjogren’s syndrome, AAV-AQP1;

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- continuing our current research programs, our preclinical development of product candidates from our current research programs and further developing our gene regulation technology;
- seeking to identify, assess, acquire and/or develop additional research programs and additional product candidates;
- the preclinical testing and clinical trials for any product candidates we identify and develop;
- establishing a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, EMA and other regulatory authorities;
- the cost of expanding and protecting our intellectual property portfolio, including filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or any of our product candidates;
- the effect of competing technological and market developments;
- the cost of further developing and scaling our manufacturing facility and processes;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the cost of making royalty, milestone or other payments under current and any future in-license agreements;
- the extent to which we in-license or acquire other products and technologies;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates in regions where we choose to commercialize our products; and
- the initiation, progress, timing and results of our commercialization of our product candidates, if approved for commercial sale.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or potentially discontinue operations.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common shareholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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***We are heavily dependent on the success of our most advanced product candidates, AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, which are still in development, and if none of them receive regulatory approval or are successfully commercialized, our business may be harmed.***

To date, we have invested a significant portion of our efforts and financial resources in the development of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1. Our future success and ability to generate product revenue is substantially dependent on our ability to successfully develop, obtain regulatory approval for and successfully commercialize these product candidates. We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect to invest a meaningful portion of our efforts and expenditures over the next few years in AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, which will require additional clinical development, management of clinical and manufacturing activities, regulatory approval in multiple jurisdictions, manufacturing sufficient supply, building of a commercial organization, substantial investment and significant marketing efforts before we can generate any revenues from any commercial sales. Accordingly, our business currently depends heavily on the successful development, regulatory approval and commercialization of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, which may never occur. We cannot be certain that AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 or AAV-AQP1 will be successful in clinical trials, receive regulatory approval or be successfully commercialized even if we receive regulatory approval. Even if we receive approval to market AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 or AAV-AQP1 from the FDA, EMA or other regulatory bodies, we cannot be certain that our product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. Additionally, the research, testing, manufacturing, labeling, approval, sale, marketing and distribution of gene therapy products are and will remain subject to extensive and evolving regulation by the FDA, EMA and other regulatory authorities. We are not permitted to market AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 or AAV-AQP1 in the United States until they receive approval of a biologics license application, or BLA, from the FDA, and we cannot market them in the European Union until we receive approval for a Marketing Authorization Application, or MAA, from the EMA, or other required regulatory approval in other countries.

AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1 are our most advanced product candidates, and because some of our other product candidates are based on similar technology, if AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 or AAV-AQP1 show unexpected adverse events or a lack of efficacy in the indications we intend to treat, or if we experience other regulatory or developmental issues, our development plans and business could be significantly harmed. Further, competitors may be developing products with similar technology and may experience problems with their products that could identify problems that would potentially harm our business.

***We may not be successful in our efforts to identify additional product candidates.***

Part of our strategy involves identifying novel product candidates. The process by which we identify product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;
- potential product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- potential product candidates may, on further study, be shown to have harmful side effects, toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance;

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- potential product candidates may not be effective in treating their targeted diseases;
- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;
- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- the regulatory pathway for a potential product candidate is too complex and difficult to navigate successfully or economically.

In addition, we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. If we are unable to identify additional suitable product candidates for clinical development, this would adversely impact our business strategy and our financial position and share price and could potentially cause us to cease operations.

***Management concluded that factors raise substantial doubt about our ability to continue as a going concern and our independent registered public accounting firm has included an explanatory paragraph relation to our ability to continue as a going concern in its report on our audited consolidated financial statements included in this prospectus.***

Our consolidated financial statements at December 31, 2016 and 2017 and March 31, 2017 and 2018 and for the periods then ended were prepared assuming that we will continue as a going concern and accordingly the accompanying financial statements do not include any adjustments that might be necessary should we be unable to continue as a going concern. However, we do not have adequate cash on hand to fund our anticipated expenses past the next 12 months without obtaining significant additional financing. This raises substantial doubt about our ability to continue as a going concern. Such determination could materially limit our ability to raise additional funds through the issuance of new debt or equity securities or otherwise. There is no assurance that sufficient financing will be available when needed to allow us to continue as a going concern. The perception that we may not be able to continue as a going concern may also make it more difficult to operate our business due to concerns about our ability to meet our contractual obligations. Our ability to continue as a going concern is contingent upon, among other factors, the sale of ordinary shares in this offering or obtaining alternate financing. We cannot provide any assurance that we will be able to raise additional capital. If we are unable to secure additional capital, we may be required to curtail our research and development initiatives and take additional measures to reduce costs in order to conserve our cash in amounts sufficient to sustain operations and meet our obligations. These measures could cause significant delays in our clinical efforts, which is critical to the realization of our business plan. It is not possible for us to predict at this time the potential success of our business. The revenue and income potential of our proposed business and operations are currently unknown. If we cannot continue as a viable entity, you may lose some or all of your investment.

In addition, the report of our independent registered public accounting firm with respect to our consolidated financial statements appearing elsewhere in this prospectus contains an explanatory paragraph stating the Company has suffered recurring losses from operations, is subject to significant uncertainty with respect to its product development and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1 to the consolidated financial statements.

## **Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval**

*We intend to identify and develop product candidates based on our novel gene therapy platform, which makes it difficult to predict the time and cost of product candidate development. Very few products that utilize transduction technology have been approved in the United States or in Europe, and there have only been a limited number of clinical trials involving a gene therapy product candidate.*

We have concentrated a portion of our research and development efforts on our gene therapy platform, which uses both transduction and gene regulation technology. Our future success depends on the successful development of these novel therapeutic approaches. To date, very few products that utilize gene transfer have been approved in the United States or Europe. There have been a limited number of clinical trials of gene transduction technologies, with only one product candidate ever approved by the FDA.

Our gene therapy platform is based on a suite of viral vectors which we can deploy with gene therapy constructs, which relies on the ability of AAV to efficiently transmit a therapeutic gene to certain kinds of cells. The mechanism of action by which these vectors target particular tissues is still not completely understood. Therefore, it is difficult for us to determine that our vectors will be able to properly deliver gene transfer constructs to, enough tissue cells to reach therapeutic levels. We cannot be certain that our viral vectors will be able to meet safety and efficacy levels needed to be therapeutic in humans or that they will not cause significant adverse events or toxicities. Furthermore, recent work conducted by a third party in non-human primates suggests that intravenous delivery of certain AAV vectors at very high doses may result in severe toxicity. The indications that we target do not use IV administration for viral vector delivery and do not use doses as high as those tested in these publications, and to date we have not observed the severe toxicities described in these publications with the naturally occurring AAV vectors that we use. However, we cannot be certain that we will be able to avoid triggering toxicities in our future preclinical studies or clinical trials. Any such results could impact our ability to develop a product candidate. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our gene therapy platform, or any similar or competitive gene therapy platforms, will result in the identification, development, and regulatory approval of any product candidates, or that other gene therapy technologies will not be considered better or more attractive. There can be no assurance that any development problems we experience in the future related to our gene therapy platform or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays and challenges in utilizing our manufacturing facility and achieving sustainable, reproducible, and scalable production. Any of these factors may prevent us from completing our preclinical studies or clinical trials or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

In addition, because our gene regulation technology is still in the research stage, we have not yet been able to assess safety in humans, and there may be long-term effects from treatment that we cannot predict at this time. Also, animal models may not exist for some of the diseases we expect to pursue.

*Because gene therapy is novel and the regulatory landscape that governs any product candidates we may develop is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.*

The regulatory requirements that will govern any novel gene therapy product candidates we develop are not entirely clear and may change. Within the broader genetic medicine field, very few therapeutic products have received marketing authorization from the EMA and FDA. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and will likely continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the

Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the United States National Institutes of Health, or the NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. The same applies in the European Union. The EMA's Committee for Advanced Therapies, or CAT, is responsible for assessing the quality, safety, and efficacy of advanced-therapy medicinal products. Advanced-therapy medicinal products include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the European Union, the development and evaluation of a gene therapy product must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any gene therapy product candidate we may develop, but that remains uncertain at this point.

Adverse developments in preclinical studies or clinical trials conducted by others in the field of gene therapy and gene regulation products may cause the FDA, the EMA, and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing gene regulation technologies, either of which could harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for product candidates such as ours can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Further, as we are developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or other regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. The prospectively designed natural history studies with the same endpoints as our corresponding clinical trials may not be accepted by the FDA, EMA or other regulatory authorities. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing gene regulation technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop.

***Clinical trials are expensive, time-consuming, difficult to design and implement, and involve an uncertain outcome. Further, we may encounter substantial delays in our clinical trials.***

The clinical trials and manufacturing of our product candidates are, and the manufacturing and marketing of our products, if approved, will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and market our product candidates. Before obtaining regulatory approvals for the commercial sale of any of our product

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candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication. In particular, because our product candidates are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

Clinical testing is expensive and can take many years to complete, and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. Failure can occur at any time during the clinical trial process. Even if our future clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of our product candidates for their targeted indications. Our future clinical trial results may not be successful.

In addition, even if such trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

To date, we have not completed any clinical trials required for the approval of our product candidates. Although we have already begun Phase 1/2 clinical trials, we may experience delays in conducting any clinical trials and we do not know whether our clinical trials will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Events that may prevent successful or timely completion of clinical development include:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation of clinical trials;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for advanced clinical trials;
- delays in developing suitable assays for screening patients for eligibility for trials with respect to certain product candidates;
- delays in reaching agreement with the FDA, EMA or other regulatory authorities as to the design or implementation of our clinical trials;
- obtaining regulatory approval to commence a clinical trial;
- reaching an agreement on acceptable terms with clinical trial sites or prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different clinical trial sites;
- obtaining institutional review board, or IRB, approval at each site;
- recruiting suitable patients to participate in a clinical trial;
- developing and validating the companion diagnostic to be used in a clinical trial, if applicable;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical sites, contract research organizations, or other third parties deviating from trial protocol or dropping out of a trial;
- failure to perform in accordance with the FDA's good clinical practice, or GCP, requirements, or applicable regulatory guidelines in other countries;



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- addressing patient safety concerns that arise during the course of a trial, including occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates or significantly increase the cost of such trials, including:

- we may experience changes in regulatory requirements or guidance, or receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate and we may not have funds to cover the costs;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- any future collaborators that conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;

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- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA, EMA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. For example, our IND for AAV-RPE65 was filed in July 2017. On August 16, 2017, we received notification from the FDA supporting the use of the described batches of product candidate in the Phase 1/2 clinical trial. However, we received a recommendation from the FDA on a certain aspect of the manufacturing process for future clinical trials, thus putting our IND for AAV-RPE65 on partial clinical hold. We responded to the FDA on October 2, 2017 and, based on this response, the partial clinical hold was lifted on October 17, 2017. As another example, our IND for AAV-CNGB3 was filed on October 31, 2017. We received a question from the FDA around our injection device compatibility assay, thus putting our AAV-CNGB3 IND on clinical hold. In the device compatibility assay, the FDA noted a disparity between the target titer for the intended low dose dilution and the actual titer obtained on polymerase chain reaction, or PCR, analysis. The FDA requested clarification on whether this was an imprecise dilution scheme for the low dose or a PCR assay issue. We submitted our second response to the FDA on May 2, 2018 providing data that identified the issue as a PCR assay artifact and also showing data that we believe supports that this has now been addressed. We may not initiate any clinical trials of AAV-CNGB3 in the United States unless and until the hold is lifted.

Our most advanced product candidates, AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, will require extensive clinical testing before we are prepared to submit a BLA or MAA for regulatory approval. We cannot predict with any certainty if or when we might complete the clinical development for our product candidates and submit a BLA or MAA for regulatory approval of any of our product candidates or whether any such BLA or MAA will be approved. We may also seek feedback from the FDA, EMA or other regulatory authorities on our clinical development program, and the FDA, EMA or such regulatory authorities may not provide such feedback on a timely basis, or such feedback may not be favorable, which could further delay our development programs.

If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be harmed, and our ability to generate revenues from our product candidates may be delayed. In addition, any delays in our clinical trials could increase our costs, slow down the development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

***The affected populations for our other product candidates may be smaller than we or third parties currently project, which may affect the addressable markets for our product candidates.***

Our projections of the number of people who have the diseases we are seeking to treat, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are estimates based on our knowledge and understanding of these diseases. The total addressable

market opportunity for our product candidates will ultimately depend upon a number of factors including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient access and product pricing and reimbursement. Incidence and prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward-looking and speculative. The process we have used in developing an estimated incidence and prevalence range for the indications we are targeting has involved collating limited data from multiple sources. Accordingly, the incidence and prevalence estimates included in this prospectus should be viewed with caution. Further, the data and statistical information used in this prospectus, including estimates derived from them, may differ from information and estimates made by our competitors or from current or future studies conducted by independent sources.

The use of such data involves risks and uncertainties and is subject to change based on various factors. Our estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of the diseases we seek to address. The number of patients with the diseases we are targeting in the United States, the European Union and elsewhere may turn out to be lower than expected or may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or access, all of which would harm our results of operations and our business.

***Negative public opinion of gene therapy and increased regulatory scrutiny of gene therapy and genetic research may adversely impact public perception of our current and future product candidates.***

Our potential therapeutic products involve introducing genetic material into patient's cells. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene therapy and gene regulation for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene regulation are unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products once approved. For example, in 2003, trials using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize murine gamma-retroviral vectors, our product candidates use a viral delivery system. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our planned or future clinical trials. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. If any such adverse events occur, commercialization of our product candidates or further advancement of our clinical trials could be halted or delayed, which would have a negative impact on our business and operations.

***Even though we have been granted access to the PRIME scheme by the EMA for AAV-CNGB3 and the FDA granted Fast Track designation to AAV-RPGR, in the future we may seek and fail to obtain access to the PRIME scheme by the EMA or fast track designation by the FDA for other of our current or potential future product candidates. We may also seek and fail to obtain breakthrough therapy designation from the FDA for our current or any future product candidates. Such designations or access may also not lead to faster development or regulatory review or approval, and it does not increase the likelihood that our product candidates will receive marketing approval.***

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of new drugs and biological products that meet certain criteria. For example, the FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs, or if the drug has been designated as a qualified infectious disease product. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. Under Fast Track, the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted if relevant criteria are satisfied, including an agreement with FDA on the proposed schedule for the submission of portions of the BLA, and the payment of applicable user fees before FDA may initiate a review. Even if Fast Track designation is granted, it may be rescinded if the product no longer meets the qualifying criteria. In April 2018, AAV-RPGR was designated a Fast Track program by the FDA for the treatment of X-linked retinitis pigmentosa owing to defects in RPGR.

In 2012, the Food and Drug Administration Safety and Innovation Act ("FDASIA"), established the breakthrough therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically-significant endpoints, such as substantial treatment effects observed early in clinical development. Sponsors may request that FDA designate a product candidate as a breakthrough therapy at the time of or any time after the submission of an IND, but ideally before an end-of-phase II meeting with FDA. If the FDA designates a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include but are not limited to holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the product candidate to ensure collection of appropriate data needed to support approval; more frequent written correspondence from the FDA about such things as the design of the proposed clinical trials and use of biomarkers; intensive guidance on an efficient drug development program, beginning as early as Phase 1; organizational commitment involving senior managers; and eligibility for rolling review and priority review. Breakthrough therapy designation comes with all of the benefits of fast track designation, which means that the sponsor may file sections of the BLA for review on a rolling basis if certain conditions are satisfied, including an agreement with FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review. Fast Track designation, priority review and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process.

Similarly, the EMA has established the PRIME scheme to expedite the development and review of product candidates that show a potential to address to a significant extent an unmet medical need, based on early clinical data. In February 2018, AAV-CNGB3 in the treatment of achromatopsia associated with defects in CNGB3 was admitted to the PRIME scheme of the EMA.

Fast Track designation and designation as a breakthrough therapy are within the discretion of the FDA. Accordingly, even if we believe one of our other product candidates meets the criteria for Fast Track designation or designation as a breakthrough therapy and we seek such designation, the FDA may disagree and instead

determine not to make such designation for such product candidate. We cannot be sure that our evaluation of our product candidates as qualifying for Fast Track designation or breakthrough therapy designation will meet the FDA's expectations. In any event, the receipt of a Fast Track designation or breakthrough therapy designation for a product candidate may not result in a faster development process, review, or approval compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if additional product candidates are granted Fast Track designation or one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Similarly, access to the PRIME scheme is at the discretion of the EMA, and we cannot be sure that any additional current or future product candidates will be granted access to the scheme; that participation in the scheme will result in expedited regulatory review or approval of our product candidates; or that access to the scheme, once granted, will not be revoked.

***We have received orphan drug designation from the FDA and EMA for AAV-CNGB3, AAV-RPE65, AAV-RPGR, AAV-AIPL1 and FDA for AAV-AQP1 and may seek orphan drug designation for additional product candidates in the future, but any orphan drug designations we have received or may receive in the future may not confer marketing exclusivity or other expected benefits.***

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating, or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits for qualified clinical testing, and user-fee waivers. In addition, if a product receives the first FDA approval of that drug for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the rare disease or condition. Under the FDA's regulations, the FDA will deny orphan drug exclusivity to a designated drug upon approval if the FDA has already approved another drug with the same active ingredient for the same indication, unless the drug is demonstrated to be clinically superior to the previously approved drug. In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following approval for the approved therapeutic indication. This period may be reduced to six years if, at the end of the fifth year, the orphan drug designation criteria are no longer met, including where it is shown that the drug is sufficiently profitable not to justify maintenance of market exclusivity. In the European Union, a marketing authorization for an orphan designated product will not be granted if a similar drug has been approved in the European Union for the same therapeutic indication, unless the applicant can establish that its product is safer, more effective or otherwise clinically superior. A similar drug is a product containing a similar active substance or substances as those contained in an already authorized product. Similar active substance is defined as an identical active substance, or an active substance with the same principal molecular structural features (but not necessarily all of the same molecular features) and which acts via the same mechanism.

We have obtained orphan drug designation from the FDA and European Commission for AAV-CNGB3 for the treatment of achromatopsia caused by mutations in the *CNGB3* gene, AAV-RPE65 for the treatment of Leber congenital amaurosis, AAV-RPGR for the treatment of retinitis pigmentosa and AAV-AIPL1 for the treatment of inherited retina dystrophy due to defects in *AIPL1* gene, and we obtained orphan drug designation from the FDA for AAV-AQP1 for the treatment of grade 2 and grade 3 late xerostomia from parotid gland hypofunction caused by radiotherapy. We plan to seek orphan drug designation for other current and future product candidates. Even with orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products, which could prevent us from marketing our product candidates if another company is able to obtain orphan drug exclusivity before we do. In addition, exclusive marketing rights in the United States may be unavailable if we seek approval for an indication broader than the orphan-designated indication or may be lost in the United States if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the drug to meet the needs of patients with the rare disease or condition following approval. Further, even if we obtain orphan drug exclusivity, that exclusivity may not effectively protect our product candidates from competition because different drugs with different active moieties can be approved for the same condition. In addition, the FDA and the EMA can subsequently approve products with the same active moiety for the same condition if the FDA or the EMA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, while we intend to seek orphan drug designation for other existing and future product candidates, we may never receive such designations. There have been legal challenges to aspects of the FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, and future challenges could lead to changes that affect the protections afforded our product candidates in ways that are difficult to predict. In 2014, a U.S. district court invalidated the FDA's denial of orphan exclusivity to an orphan designated drug, which the FDA had based on its determination that the drug was not proven to be clinically superior to a previously approved "same drug." In response to the decision, the FDA released a policy statement stating that the court's decision is limited to the facts of that particular case and that the FDA will continue to deny orphan drug exclusivity to a designated drug upon approval if the drug is the "same" as a previously approved drug, unless the drug is demonstrated to be clinically superior to that previously approved drug. Since then, similar legal challenges have been initiated against the FDA for its denial of orphan drug exclusivity to other designated drugs, and in 2017, Congress amended the Orphan Drug Act to require a demonstration of clinical superiority upon approval as a condition of receiving orphan drug exclusivity when another "same drug" has already been approved for the same indication. In the future, there is the potential for additional legal challenges to the FDA's orphan drug regulations and policies, and it is uncertain how ongoing and future challenges might affect our business.

***We and our contract manufacturer for plasmid are subject to significant regulation with respect to manufacturing our products. Our manufacturing facilities and the third-party manufacturing facility which we rely on may not continue to meet regulatory requirements and have limited capacity.***

We currently have relationships with a limited number of suppliers for the manufacturing of plasmid, a component of our viral vectors and product candidates. We completed the fit-out of our cGMP manufacturing facility in early 2018. However, if we experience slowdowns or problems with our facility and are unable to establish or scale our internal manufacturing capabilities, we will need to continue to contract with manufacturers that can produce the preclinical, clinical and commercial supply of our products. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for components our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials in

the European Union must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA or MAA on a timely basis. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could harm our business. If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be harmed. Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA and/or MAA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

***Any contamination in our manufacturing process, shortages of raw materials or failure of our plasmid supplier to deliver necessary components could result in delays in our clinical development or marketing schedules.***

Given the nature of biologics manufacturing, there is a risk of contamination. Any contamination could adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage. Some of the raw materials required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could adversely affect our development timelines and our business, financial condition, results of operations and prospects.

***If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. The natural history studies may fail to provide us with patients for our clinical trials because patients enrolled in the natural history studies may not be good candidates for our clinical trials, or may choose to not enroll in our clinical trials. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. The enrollment of patients depends on many factors, including:

- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials may compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates or approved products for the same clinical indications, and this competition may reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors, or chose to be treated using Luxturna, a commercially available product by Spark Therapeutics, Inc. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which may reduce the number of patients who are available for our clinical trials in such clinical trial site.

Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our product candidates, or could render further development impossible.

***Our product candidates may cause serious adverse events or undesirable side effects or have other properties which may delay or prevent their regulatory approval, limit the commercial profile of an approved label, or, result in significant negative consequences following marketing approval, if any.***

Serious adverse events or undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA or other authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects, toxicities or unexpected characteristics, including death. A risk in any gene therapy product based on viral vectors is the risk of insertional oncogenesis.



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If unacceptable side effects or deaths arise in the development of our product candidates, we, the FDA, the IRBs at the institutions in which our studies are conducted, DSMB, EMA or CAT could suspend or terminate our clinical trials or the FDA, EMA or other regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Undesirable side effects or deaths in clinical trials with our product candidates may cause the FDA or comparable foreign regulatory authorities to place a clinical hold on the associated clinical trials, to require additional studies, or otherwise to delay or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

If any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by any such product, including during any long-term follow-up observation period recommended or required for patients who receive treatment using our products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product;
- regulatory authorities may require additional warnings on the label, such as a “black box” warning or contraindication;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- the product could become less competitive;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

### ***Success in preclinical studies or clinical trials may not be indicative of results in future clinical trials.***

Results from previous preclinical studies or clinical trials are not necessarily predictive of future clinical trial results, and interim results of a clinical trial are not necessarily indicative of final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Frequently, product candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later clinical trials. In addition, the design of a clinical trial can

determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. There is a high failure rate for drugs and biologic products proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

***The regulatory approval processes of the FDA, EMA and other regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.***

The time required to obtain approval by the FDA, EMA and other regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our product candidates in clinical programs or any other product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States or the European Union until we receive regulatory approval of a BLA from the FDA or a MAA from the EMA, respectively. It is possible that the FDA may refuse to accept for substantive review any biologic license applications, or BLAs, or the EMA any of our MAAs, that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates.

Prior to obtaining approval to commercialize a product candidate in the United States, the European Union or elsewhere, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA, EMA or foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA, EMA or other regulatory authorities. The FDA or EMA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program. Depending on the extent of these or any other FDA or EMA required studies, approval of any regulatory approval applications that we submit may be delayed by several years, or may require us to expend significantly more resources than we have available.

Of the large number of potential products in development, only a small percentage successfully complete the FDA, EMA or other foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

***Even if we obtain FDA or EMA approval for AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 or AAV-AQP1 in the United States or European Union, we may never obtain approval for or commercialize it in any other jurisdiction, which would limit our ability to realize their full market potential.***

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy.

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Approval by the FDA in the United States or the EMA in the European Union does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

***Even if we receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.***

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising and promotional activities for such product, among other things, will be subject to extensive and ongoing requirements of and review by the FDA, EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and GCP requirements for any clinical trials that we conduct post-approval.

The FDA and EMA closely regulate the post-approval marketing and promotion of genetic therapy medicines to ensure they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and EMA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market our products for uses beyond their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the U.S. federal Food, Drug, and Cosmetic Act, or FDCA, relating to the promotion of prescription drugs may lead to FDA enforcement actions and investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;

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- warning letters or holds on clinical trials;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure or detention; or
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and biologics and spur innovation and contains provisions applicable to the development of gene therapies, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

***Interim "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publish interim "top-line" or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

#### **Risks Related to Healthcare Laws and Other Legal Compliance Matters**

***Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.***

In the United States, the European Union and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- new requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting “transfers of value” made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer’s Medicaid rebate liability;
- a licensure framework for follow on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Most recently, the Tax Cuts and Jobs Act of 2017 was enacted, which includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. The current Trump administration and Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. It is uncertain the extent to which any such changes may impact our business or financial condition.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, led to aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2027 unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. The Trump administration’s budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement

of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved.

In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the European Union or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

***Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.***

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal civil and criminal false claims and civil monetary penalties laws, including the civil False Claims Act, which prohibit, among other things, , including through civil whistleblower or qui tam actions, individuals or entities from knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes which prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program,

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or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as certain health plans, healthcare clearinghouses and healthcare providers as well as their business associates, independent contractors of a covered entity that perform certain services involving the use or disclosure of individually identifiable health information;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- similar healthcare laws and regulations in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting



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obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

***We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.***

Our operations, including our development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third-party manufacturers or our development efforts may be interrupted or delayed.

***Due to our international operations, we are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses.***

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act; the U.S. Foreign Corrupt Practices Act, or FCPA; and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA, and these other laws generally prohibit us, our officers and our employees and intermediaries from bribing, being bribed by, or providing prohibited payments or anything else of value to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA, or local anti-corruption laws. In addition, we cannot predict the nature, scope, or effect of future regulatory requirements to which any of our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We also are subject to other laws and regulations governing any international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the EU, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, or, collectively, the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA, or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA, and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement, and other sanctions and

remedial measures and legal expenses. Any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws, or Trade Control laws by U.K., U.S., or other authorities, even if it is ultimately determined that we did not violate such laws, could be costly and time-consuming, require significant personnel resources, and harm our reputation.

We will seek to build and continuously improve our systems of internal controls and to remedy any weaknesses identified. There can be no assurance, however, that the policies and procedures will be followed at all times or effectively detect and prevent violations of the applicable laws by one or more of our employees, consultants, agents, or collaborators and, as a result, we could be subject to fines, penalties, or prosecution.

#### **Risks Related to Commercialization**

***We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.***

The development and commercialization of new gene therapy products is highly competitive. Moreover, the gene regulation and manufacturing fields are characterized by rapidly changing technologies, significant competition, and a strong emphasis on intellectual property. We will face competition with respect to any product candidates that we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs, including inherited retinal diseases and neurodegenerative diseases. Some of these competitive products and therapies are based on scientific approaches that are similar to our approach, and others are based on entirely different approaches.

Our platform and products focus on the development of gene therapies and gene regulation technology. There are a number of companies developing gene therapy products include Applied Genetic Technologies Corporation, Nightstar Therapeutics plc and Spark Therapeutics, Inc. In addition to competition from other gene therapies, any products we may develop may also face competition from other types of therapies, such as small molecule, antibody, protein or other therapies.

Many of our current or potential competitors, either alone or with their collaboration partners, have greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non-competitive. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able

to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomic or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

***The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

The availability of coverage and adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates, assuming FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for our products or procedures using our products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. Obtaining coverage and adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Separate reimbursement for the product itself or the treatment or procedure in which our product is used may not be available. A decision by a third-party payor not to cover or separately reimburse for our products or procedures using our products, could reduce physician utilization of our products once approved. Assuming there is coverage for our product candidates or procedures using our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially-reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

***Even if our product candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success.***

If our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If they do not achieve an adequate level of acceptance, we may not generate significant product revenues or become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;

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- the availability of third-party coverage and adequate reimbursement;
- product labeling or product insert requirements of the FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product together with other medications.

Because we expect sales of our product candidates, if approved, to generate substantially all of our product revenues for a substantial period, the failure of this product to find market acceptance would harm our business and could require us to seek additional financing.

***If we are unable to establish sales, marketing and distribution capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates or realizing the synergies in the target indications of our programs, even if they are approved.***

We do not have any infrastructure for the sales, marketing or distribution of our products, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. We expect to build a focused sales, distribution and marketing infrastructure to market our product candidates in the United States and European Union, if approved. There are significant expenses and risks involved with establishing our own sales, marketing and distribution capabilities, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could delay any product launch, which would adversely impact the commercialization of our product candidates. Additionally, if the commercial launch of our product candidates for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

We may not have the resources in the foreseeable future to allocate to the sales and marketing of our product candidates in certain international markets. Therefore, our future sales in these markets will largely depend on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator's strategic interest in the product and such collaborator's ability to successfully market and sell the product. We may pursue collaborative arrangements regarding the sale and marketing of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, if approved, for certain markets overseas; however, we cannot assure that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that they will have effective sales forces.

If we are unable to build our own sales force or negotiate a collaborative relationship for the commercialization of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, we may be forced to delay the potential commercialization of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1 or reduce the scope of our sales or marketing activities for AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1. If we elect to increase our expenditures to fund commercialization activities internationally, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. We could enter into arrangements with collaborative partners at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1 or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business, operating results and prospects.

Some indications targeted by our ophthalmology programs are rare, but we anticipate realizing synergies in commercializing of our IRD product candidates, should they be approved. Failure to realize synergies in our sales, marketing and distribution efforts may harm our commercialization efforts.

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If we are unable to establish adequate sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1 and may not become profitable and may incur significant additional losses. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

***If we obtain approval to commercialize any products outside of the United States or the European Union, a variety of risks associated with international operations could adversely affect our business.***

If AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1 are approved for commercialization, we intend to enter into agreements with third parties to market it in certain jurisdictions outside the United States and the European Union. We expect that we will be subject to additional risks related to international pharmaceutical operations, including:

- different regulatory requirements for drug and biologic approvals and rules governing drug and biologic commercialization in foreign countries;
- reduced protection for intellectual property rights;
- foreign reimbursement, pricing and insurance regimes;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability;
- greater difficulty with enforcing our contracts;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions; and
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by individual countries in Europe with which we will need to comply. If we are unable to successfully manage the challenges of international expansion and operations, our business and operating results could be harmed.

***Any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.***

The ACA includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or

interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own pre-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have an adverse effect on the future commercial prospects for our biological products.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

### **Risks Related to Our Dependence on Third Parties**

***If our recently completed cGMP manufacturing facility is unable to supply our product candidates for all of our current preclinical, clinical and potential commercial needs, we will be forced to seek out third-party manufacturers. We currently contract with third parties for the manufacture of plasmid used in producing our product candidates. Relying on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.***

We have begun producing our product candidates in our facility. However, if our facility is damaged, suffers any form of delay or regulatory challenges, or we are unable to scale our internal manufacturing capabilities to meet demand for our product candidates, we will need to contract with third-party manufacturers to produce our product candidates.

We currently rely on third-party manufacturers for the manufacture of plasmid used in the production of our product candidates. We do not have a long term supply agreement with any of the third-party manufacturers, and we purchase our required supply on a purchase order basis.

We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting.

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Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements that might be required by the FDA or EMA. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could adversely affect supplies of our candidates and harm our business, financial condition, results of operations, and prospects.

Any therapies that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop or any components required for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

***We may collaborate with third parties for the development and commercialization of our product candidates. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all.***

We may seek collaborative relationships for the development and commercialization of our product candidates. Failure to obtain a collaborative relationship for our product candidates may significantly impair their commercial potential. We also may need to enter into collaborative relationships to provide funding to support our other research and development programs. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, such as:

- a collaboration partner may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale or downsizing;
- a collaboration partner may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- a collaboration partner may cease development in therapeutic areas which are the subject of our strategic collaboration;
- a collaboration partner may not devote sufficient capital or resources towards our product candidates;
- a collaboration partner may change the success criteria for a product candidate thereby delaying or ceasing development of such candidate;
- a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaboration partner could develop a product that competes, either directly or indirectly, with our product candidate;
- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;



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- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaboration partner may terminate a strategic alliance;
- a dispute may arise between us and a partner concerning the research, development or commercialization of a product candidate resulting in a delay in milestones, royalty payments or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- a partner may use our products or technology in such a way as to make us subject to litigation with a third party.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital. Moreover, any collaborative partners we enter into agreements with in the future may shift their priorities and resources away from our product candidates or seek to renegotiate or terminate their relationships with us.

### **Risks Related to Intellectual Property**

***We depend on proprietary technology licensed from others. If we lose our existing licenses or are unable to acquire or license additional proprietary rights from third parties, we may not be able to continue developing our product candidates.***

We currently in-license certain intellectual property from UCL Business, Plc, or UCLB, and Brandeis University, or Brandeis. We are a party to agreements with UCL for certain technology and AAV vector-related patents and with Brandeis for certain preclinical technology for the treatment of ALS, and we may enter into additional agreements, including license agreements, with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us. For example, in exchange for the rights granted to us by UCL, we are obligated to pay an annual management fee, milestone payments for certain commercial sales thresholds, and a certain percentages of proceeds on sublicensing revenues. If we fail to comply with our obligations to UCL, Brandeis, or any of our other collaborators, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, which could adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

We may rely on other third parties from whom we license proprietary technology to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We may have limited control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We may have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that may be licensed to us. It is possible that the licensors' infringement proceeding or

defense activities may be less vigorous than if we conduct them ourselves. The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. Furthermore, we may be unable to in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties, which we identify as necessary for our product candidates.

***If we are unable to obtain and maintain patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.***

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our proprietary technologies, product candidate development programs and product candidates. Our success depends in large part on our ability to secure and maintain patent protection in the United States and other countries with respect to our current product candidates and any future product candidates we may develop. We seek to protect our proprietary position by filing or collaborating with our licensors to file patent applications in the United States and abroad related to our proprietary technologies, development programs and product candidates. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Moreover, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our proprietary products and technology, including current product candidates, any future product candidates we may develop, and our gene regulation technology in the United States or in other foreign countries, in whole or in part. Alternately, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending patent application or later invalidate or narrow the scope of an issued patent. For example, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Even if patents do successfully issue and even if such patents cover our current product candidates, any future product candidates we may develop and our gene regulation technology, third parties may challenge their validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful challenge to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any of our product candidates or gene regulation technology. Our competitors may be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate and our gene regulation technology under patent protection could be reduced.

If the patent applications we hold or have in-licensed with respect to our development programs and product candidates fail to issue, if their validity, breadth or strength of protection is threatened, or if they fail to

provide meaningful exclusivity for any of our current or future product candidates or technology, it could dissuade companies from collaborating with us to develop product candidates, encourage competitors to develop competing products or technologies and threaten our ability to commercialize future product candidates. Any such outcome could harm our business.

The patent position of biotechnology and pharmaceutical companies is highly uncertain, involves complex legal and factual questions, and is characterized by the existence of large numbers of patents and frequent litigation based on allegations of patent or other intellectual property infringement or violation. In addition, the laws of jurisdictions outside the United States may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. Since patent applications in the United States and other jurisdictions are confidential for a period of time after filing, we cannot be certain that we were the first to file for patents covering our inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in the issuance of patents, or may result in the issuance of patents which fail to protect our technology or products, in whole or in part, or which fail to effectively prevent others from commercializing competitive technologies and products.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Thus, even if our patent applications issue as patents, they may not issue in a form that will provide us with meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however the life of a patent, and the protection it affords, is limited. Without patent protection for our current or future product candidates, we may be open to competition from generic versions of such products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

***Third parties may assert claims against us alleging infringement of their patents and proprietary rights, or we may need to become involved in lawsuits to defend or enforce our patents, either of which could result in substantial costs or loss of productivity, delay or prevent the development and commercialization of our product candidates, prohibit our use of proprietary technology or sale of products or put our patents and other proprietary rights at risk.***

Our commercial success depends, in part, upon our ability to develop, manufacture, market and sell our product candidates without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Litigation relating to infringement or misappropriation of patent and other intellectual property rights in the pharmaceutical and biotechnology industries is common, including patent infringement lawsuits, interferences, oppositions and *inter partes* reviews, and reexamination proceedings before the U.S. Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including the biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an

advantage over their competitors. Numerous U.S., EU and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates, and as the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us.

We may be subject to third-party claims including infringement, interference or derivation proceedings, post-grant review and inter partes review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Even if such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize the applicable product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. There may be third-party patents or patent applications with claims to compositions, formulations, or methods of treatment, prevention use, or manufacture of our product candidates or technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to prohibit our use of those compositions, formulations, methods of treatment, prevention or use or other technologies, effectively blocking our ability to develop and commercialize the applicable product candidate until such patent expires or is finally determined to be invalid or unenforceable or unless we obtained a license.

In addition, defending such claims would cause us to incur substantial expenses and, if successful, could cause us to pay substantial damages if we are found to be infringing a third party's patent rights. These damages potentially include increased damages (possibly treble damages) and attorneys' fees if we are found to have infringed such rights willfully. Further, if a patent infringement suit is brought against us or our third-party service providers, our development, manufacturing or sales activities relating to the product or product candidate that is the subject of the suit may be delayed or terminated. As a result of patent infringement claims, or in order to avoid potential infringement claims, we may choose to seek, or be required to seek, a license from the third party, which may require payment of substantial royalties or fees, or require us to grant a cross-license under our intellectual property rights. These licenses may not be available on reasonable terms or at all. Even if a license can be obtained on reasonable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we could be prevented from commercializing one or more of our product candidates, or forced to modify such product candidates, or to cease some aspect of our business operations, which could harm our business significantly. We might also be forced to redesign or modify our product candidates so that we no longer infringe the third-party intellectual property rights, which may result in significant cost or delay to us, or which redesign or modification could be impossible or technically infeasible. Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. In addition, if the breadth or strength of protection provided the patents and patent applications we own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Competitors may infringe our patents or other intellectual property. If we or one of our licensors were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of

novelty, obviousness lack of written description, or non-enablement. Third parties might allege unenforceability of our patents because during prosecution of the patent an individual connected with such prosecution withheld relevant information, or made a misleading statement. Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution, but that an adverse third party may identify and submit in support of such assertions of invalidity. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors view these announcements in a negative light, the price of our ordinary shares could be adversely affected. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace.

***We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop, manufacture and market our product candidates.***

We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, in the United States, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States, the European Union and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could be filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States, the European Union or elsewhere that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

If we fail to correctly identify or interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay monetary damages, we may be temporarily or permanently prohibited from commercializing our product candidates. We might, if possible, also be forced to redesign our product candidates in a manner that no longer infringes third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

***Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.***

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and genetic medicine industries involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biotechnology and genetic medicine patents is costly, time-consuming and inherently uncertain. In addition, the Leahy-Smith America Invents Act, or the AIA, which was passed in September 2011, resulted in significant changes to the U.S. patent system.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned from a “first-to-invent” to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. Under a “first-to-file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application and diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. It is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors’ patent applications and the enforcement or defense of our or our licensors’ issued patents.

We may become involved in opposition, interference, derivation, inter partes review or other proceedings challenging our or our licensors’ patent rights, and the outcome of any proceedings are highly uncertain. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our owned or in-licensed patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in

certain situations, and there are other open questions under patent law that courts have yet to decisively address. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution, but, the complexity and uncertainty of European patent laws has also increased in recent years. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

The USPTO, European and other patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO, European and other patent agencies over the lifetime of a patent. While an inadvertent failure to make payment of such fees or to comply with such provisions can in many cases be cured by additional payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance with such provisions will result in the abandonment or lapse of the patent or patent application, and the partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product candidates or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, it can create opportunities for competitors to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

***We enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.***

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In-licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. And in-licensing or filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement is not as strong as that in the United States or the European Union. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened requirement for patentability and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other

proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the European Union, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets or other forms of intellectual property, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put at risk our or our licensors' patents of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail, damages or other remedies awarded to us, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those jurisdictions.

In some jurisdictions, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

***Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.***

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. Even if we or our licensors obtain patents covering our product candidates, when the terms of all patents covering a product expire, our business may become subject to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review and approval of new product candidates, patents protecting such candidates may expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.



***If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of marketing exclusivity for our product candidates, our business may be harmed.***

In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. In the European Union, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

***Our proprietary rights may not adequately protect our technologies and product candidates, and do not necessarily address all potential threats to our competitive advantage.***

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make products that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- others, including inventors or developers of our owned or in-licensed patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our technologies without infringing our intellectual property rights;
- we or our licensors or our other collaboration partners might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we own, license or will own or license;
- we or our licensors or our other collaboration partners might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license;
- we or our licensors may fail to meet obligations to the U.S. government with respect to in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents;

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- issued patents that we own or exclusively license may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership, validity or enforceability of our or our licensors' patents or patent applications may be challenged by third parties; and
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business.

***Our reliance on third parties may require us to share our trade secrets, which increases the possibility that our trade secrets will be misappropriated or disclosed, and confidentiality agreements with employees and third parties may not adequately prevent disclosure of trade secrets and protect other proprietary information.***

We consider proprietary trade secrets, confidential know-how and unpatented know-how to be important to our business. We may rely on trade secrets and confidential know-how to protect our technology, especially where patent protection is believed by us to be of limited value. However, trade secrets and confidential know-how are difficult to protect, and we have limited control over the protection of trade secrets and confidential know-how used by our licensors, collaborators and suppliers. Because we have relied in the past on third parties to manufacture our product candidates, because we may continue to do so in the future, and because we expect to collaborate with third parties on the development of our current product candidates and any future product candidates we develop, we may, at times, share trade secrets with them. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Under such circumstances, trade secrets and confidential know-how can be difficult to maintain as confidential.

To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with us prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. The need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our competitive position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have an adverse effect on our business and results of operations. Enforcing a claim that a third party obtained illegally and is using trade secrets and/or confidential know-how is expensive, time consuming and unpredictable, and the enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. Courts outside the United States are sometimes less willing to protect proprietary information, technology and know-how.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may

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discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

***If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.***

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our trademark MeiraGTx has been registered in the EU and a U.S. application is pending. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

***We may need to license additional intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.***

The growth of our business may depend in part on our ability to acquire or in-license additional proprietary rights. For example, our programs may involve product candidates that may require the use of additional proprietary rights held by third parties. Our product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may develop products containing our compositions and pre-existing pharmaceutical compositions. These pharmaceutical products may be covered by intellectual property rights held by others. We may be required by the FDA, EMA or other foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates. These diagnostic test or tests may be covered by intellectual property rights held by others. We may be unable to acquire or in-license any relevant third-party intellectual property rights that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license under such intellectual property rights, any such license may be non-exclusive, which may allow our competitors access to the same technologies licensed to us.

***We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties.***

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. Although we seek to protect our ownership of intellectual property rights by ensuring that our agreements with our employees, collaborators and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and if we fail in

defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful, litigation could result in substantial cost and reputational loss and be a distraction to our management and other employees.

### **Risks Related to Employee Matters and Managing Growth**

***We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.***

As of March 31, 2018, we had 59 full-time employees. We will need to significantly expand our organization, and we may have difficulty identifying, hiring and integrating new personnel. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our potential ability to generate revenue could be reduced and we may not be able to implement our business strategy. Many of the biotechnology companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer history in the industry than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can discover and develop product candidates and operate our business will be limited.

***Our future success depends on our ability to retain our key personnel and to attract, retain and motivate qualified personnel.***

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Alexandria Forbes, Ph.D., our President and Chief Executive Officer, Rich Giroux, our Chief Operating Officer and Stuart Naylor, Ph.D., our Chief Development Officer, as well as the other principal members of our management, scientific and clinical teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time and, for certain of our executive officers, entitle them to receive severance payments in connection with their voluntary resignation of employment. Additional details regarding these arrangements can be found in the section “Executive Compensation—Executive Compensation Arrangements.”

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the

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competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

***We expect to grow our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product candidate development, regulatory affairs and sales, marketing and distribution. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our inability to effectively manage the expansion of our operations may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees.

***Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.***

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- significant costs to defend the related litigation and related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize our product candidates;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- decreased demand for our product candidates, if approved for commercial sale; and
- loss of revenue.

***Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.***

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, clinical trial liability, employment practices liability, property, auto, workers' compensation, umbrella, and directors' and officers' insurance.

Any additional product liability insurance coverage we acquire in the future, may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for our product candidates, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the commercialization of any product candidates we develop. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

We also expect that operating as a public company will make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations.

***Our employees and independent contractors, including consultants, vendors, and any third parties we may engage in connection with development and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could harm our business.***

Misconduct by our employees and independent contractors, including consultants, vendors, and any third parties we may engage in connection with development and commercialization, could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, EMA and other similar regulatory authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject

to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

***Our business and operations would suffer in the event of system failures.***

Our computer systems, as well as those of our contractors and consultants, are vulnerable to damage from computer viruses, unauthorized access, natural disasters (including hurricanes), terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product candidate development programs. For example, the loss of preclinical study or clinical trial data from completed, ongoing or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, or breached due to employee error, a technical vulnerability, malfeasance or other disruptions. Although, to our knowledge, we have not experienced any such material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, significant regulatory penalties, and such an event could disrupt our operations, damage our reputation, and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay clinical development of our product candidates.

***We may engage in acquisitions that could disrupt our business, cause dilution to our shareholders or reduce our financial resources.***

In the future, we may enter into transactions to acquire other businesses, products or technologies. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our ordinary shares or other equity securities to the shareholders of the acquired company, which would reduce the percentage ownership of our existing shareholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

***The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our shares.***

Following the vote of a majority of the eligible members of the electorate in the United Kingdom to withdraw from the European Union in a national referendum held on June 23, 2016, the U.K. government served notice under Article 50 of the Treaty of the European Union on March 29, 2017 to formally initiate a withdrawal process. The United Kingdom and the European Union have a two-year period under Article 50 to negotiate the terms for withdrawal. Any extension of the negotiation period for withdrawal will require the consent of all of the remaining 27 member states. The referendum and withdrawal have created significant uncertainty about the future relationship between the United Kingdom and the European Union. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU-derived laws and regulations to replace or replicate as part of a withdrawal, including healthcare and pharmaceutical regulations; financial laws and regulations; tax and free trade agreements; intellectual property rights; supply chain logistics; environmental, health, and safety laws and regulations; immigration laws; and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity, and restrict our access to capital. If the United Kingdom and the European Union are unable to negotiate acceptable withdrawal terms or if other EU member states pursue withdrawal, barrier-free access between the U.K. and other EU member states or among the European economic area overall could be diminished or eliminated. These developments, or the perception that any of them could occur, have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates, and credit ratings may be especially subject to increased market volatility. In addition, changes to U.K. border and immigration policy could occur as a result of the United Kingdom's withdrawal from the European Union, affecting our ability to recruit and retain employees from outside the United Kingdom. Any of these factors could have an adverse effect on our business, financial condition, results of operations, and prospects.

Further, the vote for the United Kingdom's withdrawal from the European Union has resulted in a decision to move the EMA from the United Kingdom to the Netherlands, with operations currently scheduled to begin in the Netherlands by end of March 2019. This transition may cause disruption in the administrative and medical scientific links between the EMA and the UK Medicines and Healthcare products Regulatory Agency, or the MHRA, including delays in granting clinical trial authorization or marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of products in the European Union and/or the United Kingdom.

***Exchange rate fluctuations may adversely affect our results of operations and financial condition.***

Owing to the international scope of our operations, fluctuations in exchange rates, particularly between the pound sterling and the U.S. dollar, may adversely affect us. Although some of our operations are based in the United Kingdom, we source research and development, manufacturing, consulting and other services from the United States and the European Union. Further, potential future revenue may be derived from abroad, particularly from the United States. As a result, our business and the market price of our securities may be affected by fluctuations in foreign exchange rates not only between the pound sterling and the U.S. dollar, but also the euro, which may have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place.



## **Risks Related to Our Ordinary Shares and this Offering**

### ***An active trading market for our ordinary shares may not develop.***

Prior to this offering, there has been no public market for our ordinary shares. Although we have applied to have our ordinary shares approved for listing on The Nasdaq Global Market, or Nasdaq, an active trading market for our shares may never develop or be sustained following this offering. Any delay in the commencement of trading of our ordinary shares on Nasdaq would impair the liquidity of the market for our ordinary shares and make it more difficult for holders to sell their shares. The initial public offering price for our ordinary shares will be determined through negotiations with the underwriters. Among the factors considered in determining the initial public offering price were our future prospects and the prospects of our industry in general, our revenue, net income and certain other financial and operating information in recent periods, and the market prices of securities and certain financial and operating information of companies engaged in activities similar to ours. If an active market for our ordinary shares does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares, or at all.

### ***The market price of our ordinary shares may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our ordinary shares in this offering.***

Our share price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your ordinary shares at or above the initial public offering price. The market price for our ordinary shares may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of clinical trials of our product candidates or those of our competitors;
- developments related to our existing or any future collaborations;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;
- announcements by us, our partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;

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- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions;
- changes in accounting principles; and
- the other factors described in this “Risk Factors” section and elsewhere in this prospectus.

In addition, the stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, when the market price of a security has been volatile, holders of that security have sometimes instituted securities class action litigation against the issuer. If any of the holders of our ordinary shares were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our senior management would be diverted from the operation of our business. Any adverse determination in litigation could also subject us to significant liabilities. Broad market and industry factors may negatively affect the market price of our ordinary shares, regardless of our actual operating performance. Further, a decline in the financial markets and related factors beyond our control may cause the price of our ordinary shares to decline rapidly and unexpectedly. If the market price of our ordinary shares after the completion of this offering does not exceed the initial public offering price, you may not realize any return on your investment in us and may lose some or all of your investment.

***After this offering, our executive officers, directors and principal shareholders, if they choose to act together, will continue to have the ability to control or significantly influence all matters submitted to shareholders for approval.***

Upon the closing of this offering, based on the number of ordinary shares outstanding as of \_\_\_\_\_, 2018, our executive officers, directors and shareholders who owned more than 5% of our outstanding ordinary shares before this offering and their respective affiliates will, in the aggregate, hold ordinary shares representing approximately \_\_\_\_\_% of our outstanding ordinary shares. In addition, upon the closing of this offering, based on the number of ordinary shares outstanding as of \_\_\_\_\_, 2018, Kadmon Corporation, LLC owned \_\_\_\_\_% of our outstanding ordinary shares before this offering and will own hold ordinary shares representing approximately \_\_\_\_\_% of our outstanding voting shares.

As a result, if these shareholders choose to act together, they would be able to control or significantly influence all matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors, the composition of our management and approval of any merger, consolidation, sale of all or substantially all of our assets or other business combination that other shareholders may desire. Any of these actions could adversely affect the market price of our ordinary shares.

***If you purchase ordinary shares in this offering, you will suffer immediate dilution of your investment.***

The initial public offering price of our ordinary shares will be substantially higher than the net tangible book value per share of our ordinary shares. Therefore, if you purchase our ordinary shares in this offering, you

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will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent shares subsequently are issued under outstanding options or warrants or to executive officers in connection with this offering, you will incur further dilution. Based on an assumed initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, you will experience immediate dilution of \$ \_\_\_\_\_ per share as of \_\_\_\_\_, 2018, representing the difference between our pro forma as adjusted net tangible book value per share, after giving effect to this offering, and the assumed initial public offering price. In addition, purchasers of ordinary shares in this offering will have contributed approximately \_\_\_\_\_ % of the aggregate price paid by all purchasers of our ordinary shares but will own only approximately \_\_\_\_\_ % of our ordinary shares outstanding after this offering.

***We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.***

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our ordinary shares. We expect that we will use the net proceeds of this offering to advance our clinical and preclinical programs, develop our gene regulation technology, invest in our vector design and production platform, build-out our internal manufacturing capacity, expand our intellectual property portfolio and pursue additional research and development activities as set forth under “Use of Proceeds.” However, our use of these proceeds may differ substantially from our current plans. The failure by our management to apply these funds effectively could result in financial losses that could have a negative impact on our business, cause the price of our ordinary shares to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

***A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our ordinary shares to drop significantly, even if our business is doing well.***

Sales of a substantial number of our ordinary shares in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our ordinary shares. After this offering, we will have outstanding \_\_\_\_\_ ordinary shares (or \_\_\_\_\_ ordinary shares if the underwriters’ exercise their option to purchase additional ordinary shares in full). This includes the shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. The remaining \_\_\_\_\_ ordinary shares will be restricted as a result of securities laws or lock-up agreements but will become eligible to be sold after this offering as described in the “Shares Eligible for Future Sale” and “Underwriting” sections of this prospectus. Moreover, after this offering, holders of an aggregate of \_\_\_\_\_ ordinary shares will have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other shareholders, until such shares can otherwise be sold without restriction under Rule 144 or until the rights terminate pursuant to the terms of the shareholders agreement between us and such holders. We also intend to register approximately \_\_\_\_\_ ordinary shares subject to equity awards issued or reserved for future issuance under our equity compensation plans on a registration statement on Form S-8. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described above. Any sales of securities by these shareholders could have a negative impact on the trading price of our ordinary shares.

***We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our ordinary shares less attractive to investors.***

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of the closing of this offering. However, if certain events occur prior to the end of such five-year period, including if we become a “large accelerated filer,” our annual gross revenues exceed

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\$1.07 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure in this prospectus;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our ordinary shares less attractive if we rely on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may be reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

***We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.***

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the Nasdaq listing requirements and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

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Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our ordinary shares, our share price and trading volume could decline.***

The trading market for our ordinary shares will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have, and may never obtain, research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our shares could be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our share performance, or if any of our preclinical studies or clinical trials and operating results fail to meet the expectations of analysts, our share price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our share price or trading volume to decline.

***Anti takeover provisions in our organizational documents and Cayman Islands law may discourage or prevent a change of control, even if an acquisition would be beneficial to our shareholders, which could depress the price of our ordinary shares and prevent attempts by our shareholders to replace or remove our current management.***

Our memorandum and articles of association contain provisions that may discourage unsolicited takeover proposals that shareholders may consider to be in their best interests. Our board of directors is divided into three classes with staggered, three year terms. Our board of directors has the ability to designate the terms of and issue preferred shares without shareholder approval. We are also subject to certain provisions under Cayman Islands law that could delay or prevent a change of control. Together these provisions may make more difficult the removal of management and may discourage transactions that otherwise could involve payment of a premium over prevailing market prices for our ordinary shares. See “Description of Share Capital.”

***There may be difficulties in enforcing foreign judgments against our management or us.***

Certain of our directors and management and certain of the other parties named in this prospectus reside outside the United States. A significant portion of our assets and such persons’ assets are located outside the United States. As a result, it may be difficult or impossible for investors to effect service of process upon us within the United States or other jurisdictions, including judgments predicated upon the civil liability provisions of the federal securities laws of the United States. See “Enforcement of Civil Liabilities.”

In particular, investors should be aware that there is uncertainty as to whether the courts of the Cayman Islands or any other applicable jurisdictions would recognize and enforce judgments of U.S. courts obtained

against us or our directors or management as well as against the selling shareholders predicated upon the civil liability provisions of the securities laws of the United States or any state in the United States or entertain original actions brought in the Cayman Islands or any other applicable jurisdictions courts against us or our directors or officers as well as against the selling shareholders predicated upon the securities laws of the United States or any state in the United States.

***The rights of our shareholders differ from the rights typically offered to shareholders of a U.S. corporation.***

Our corporate affairs and the rights of holders of ordinary shares are governed by Cayman Islands law, including the provisions of the Cayman Islands Companies Law (2018 Revision), or the Companies Law, the common law of the Cayman Islands and by our memorandum and articles of association. We will also be subject to the federal securities laws of the United States. The rights of shareholders to take action against the directors, actions by minority shareholders and the fiduciary responsibilities of our directors to us under Cayman Islands law are to a large extent governed by the common law of the Cayman Islands. The common law of the Cayman Islands is derived in part from comparatively limited judicial precedent in the Cayman Islands as well as from English common law, the decisions of whose courts are of persuasive authority, but are not binding on a court in the Cayman Islands. The rights of our shareholders and the fiduciary responsibilities of our directors under Cayman Islands law are different from what they would be under statutes or judicial precedent in some jurisdictions in the United States. In particular, the Cayman Islands has a different body of securities laws as compared to the United States, and certain states, such as Delaware, may have more fully developed and judicially interpreted bodies of corporate law. In addition, Cayman Islands companies may not have standing to initiate a shareholders derivative action in a Federal court of the United States. See “Description of Share Capital and Articles of Association—Differences in Corporate Law” in this prospectus for a description of the principal differences between the provisions of the Companies Law applicable to us and, for example, the Delaware General Corporation Law relating to shareholders’ rights and protections.

As a result of all of the above, public shareholders may have more difficulty in protecting their interests in the face of actions taken by management, members of the board of directors or controlling shareholders than they would as public shareholders of a United States company.

***If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ordinary shares.***

Section 404(a) of the Sarbanes-Oxley Act, or Section 404(a), requires that beginning with our second annual report following our initial public offering, management assess and report annually on the effectiveness of our internal control over financial reporting and identify any material weaknesses in our internal control over financial reporting. Although Section 404(b) of the Sarbanes-Oxley Act, or Section 404(b), requires our independent registered public accounting firm to issue an annual report that addresses the effectiveness of our internal control over financial reporting, we have opted to rely on the exemptions provided in the JOBS Act, and consequently will not be required to comply with SEC rules that implement Section 404(b) until such time as we are no longer an “emerging growth company.”

We expect our first Section 404(a) assessment will take place for our annual report for the fiscal year ending December 31, 2019. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material

weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inadequate internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our ordinary shares.

***Because we do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future, capital appreciation, if any, would be your sole source of gain.***

Under current U.K. law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be paid. Therefore, we must have distributable profits before issuing a dividend. We have never declared or paid any cash dividends on our ordinary shares. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our ordinary shares would be your sole source of gain on an investment in our ordinary shares for the foreseeable future. See the "Dividend Policy" section of this prospectus for additional information.

***We could be subject to securities class action litigation.***

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

***We expect to be treated as resident in the United Kingdom for tax purposes, but may be treated as a dual resident company for United Kingdom tax purposes.***

It is the intention of our board of directors to conduct our affairs so that the central management and control of the company is exercised in the United Kingdom. As a result, we expect to be treated as resident in the United Kingdom for UK tax purposes. Accordingly, we expect to be subject to UK taxation on our income and gains, except where an exemption applies.

However, we may be treated as a dual resident company for UK tax purposes. As a result, our right to claim certain reliefs from UK tax may be restricted, and changes in law or practice in the United Kingdom could result in the imposition of further restrictions on our right to claim UK tax reliefs.

***We may be classified as a passive foreign investment company for U.S. federal income tax purposes, which could result in adverse U.S. federal income tax consequences to U.S. investors in our ordinary shares.***

Based on the current and anticipated value of our assets, including goodwill, and the composition of our income, assets and operations, we do not believe we were a "passive foreign investment company," or PFIC, for the taxable year ending on December 31, 2017, and do not expect to be a PFIC for the current taxable year. However, the application of the PFIC rules is subject to uncertainty in several respects, and we cannot assure you that the U.S. Internal Revenue Service, or the IRS, will not take a contrary position. Furthermore, a separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. Accordingly, we cannot assure you that we were not a PFIC for our taxable year ending on December 31, 2017 and that we will not be a PFIC for our current taxable year or any future taxable year. A non-U.S. company will be considered a PFIC for any taxable year if (i) at least 75% of its gross income is passive income (including interest income), or (ii) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income. If we were to be classified as a PFIC for any taxable year during which a U.S. Holder (as defined below

under “Material U.S. Federal Income Tax Consequences”) holds our ordinary shares, certain adverse U.S. federal income tax consequences could apply to such U.S. Holder, including (i) the treatment of all or a portion of any gain on disposition of our ordinary shares as ordinary income, (ii) the application of a deferred interest charge on such gain and the receipt of certain dividends and (iii) the obligation to comply with certain reporting requirements. See “Material U.S. Federal Income Tax Consequences—Passive Foreign Investment Company Rules.”

***If a United States person is treated as owning at least 10% of our ordinary shares, such holder may be subject to adverse U.S. federal income tax consequences.***

If a U.S. Holder is treated as owning (directly, indirectly or constructively) at least 10% of the value or voting power of our ordinary shares, such U.S. Holder may be treated as a “United States shareholder” with respect to each “controlled foreign corporation” in our group (if any). If our group includes one or more U.S. subsidiaries, certain of our non-U.S. subsidiaries could be treated as controlled foreign corporations (regardless of whether we are treated as a controlled foreign corporation). A United States shareholder of a controlled foreign corporation may be required to report annually and include in its U.S. taxable income its pro rata share of “Subpart F income,” “global intangible low-taxed income” and investments in U.S. property by controlled foreign corporations, regardless of whether we make any distributions. An individual that is a United States shareholder with respect to a controlled foreign corporation generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a United States shareholder that is a U.S. corporation. Failure to comply with these reporting obligations may subject you to significant monetary penalties and may prevent the statute of limitations from starting with respect to your U.S. federal income tax return for the year for which reporting was due. We cannot provide any assurances that we will assist investors in determining whether any of our non-U.S. subsidiaries is treated as a controlled foreign corporation or whether such investor is treated as a United States shareholder with respect to any of such controlled foreign corporations. Further, we cannot provide any assurances that we will furnish to any United States shareholders information that may be necessary to comply with the aforementioned reporting and tax payment obligations. U.S. Holders should consult their tax advisors regarding the potential application of these rules to their investment in our ordinary shares.

***Comprehensive tax reform legislation could adversely affect our business and financial condition.***

The U.S. government has recently enacted comprehensive tax legislation that includes significant changes to the taxation of business entities, referenced herein as the Tax Reform Act. These changes include, among others, a permanent reduction to the corporate income tax rate, limiting interest deductions and the use of net operating losses, adopting elements of a territorial tax system and introducing certain anti-base erosion provisions. We continue to examine the impact this tax reform legislation may have on our business. The effect of the Tax Reform Act on our business, whether adverse or favorable, is uncertain, and may not become evident for some period of time. U.S. Holders should consult their legal and tax advisors regarding any such legislation and the potential tax consequences of investing in our ordinary shares.

***Changes in tax laws or challenges to our tax position could adversely affect our results of operations and financial condition.***

We are subject to complex tax laws. Changes in tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate could adversely affect our tax position, including our effective tax rate or tax payments.

In October 2015, the Organization for Economic Co-Operation and Development released a final package of measures to be implemented by member nations in response to a 2013 action plan calling for a coordinated multi-jurisdictional approach to “base erosion and profit shifting” by multinational companies. Multiple member jurisdictions, including the countries in which we operate, have begun implementing recommended changes such as country-by-country reporting requirements and changes to double tax treaties.



Additional multilateral changes are anticipated in upcoming years. We often rely on generally available interpretations of applicable tax laws, treaties and regulations. There cannot be certainty that the relevant tax authorities are in agreement with our interpretation of these laws, regulations or treaties, or with tax positions that we have taken. If our interpretation or tax position is challenged by the relevant tax authorities, we could be required to pay taxes that we currently do not collect or pay, may be subject to interest and penalties and there could be an increase to the costs of our services to track and collect such taxes, which could increase our costs of operations or our effective tax rate. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a “permanent establishment” under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. The occurrence of any of the foregoing tax risks could have a material adverse effect on our business, financial condition and results of operations.

We are unable to predict what national or international tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could impact the tax treatment of our earnings, adversely affect our profitability and increase the complexity, burden and cost of tax compliance.

***We have significant net operating losses, or NOLs, and U.K. carryforward tax losses which we may not be able to realize or which may be restricted following the corporate reorganization or any future change of control. We also benefit from certain tax incentive regimes, such as research and development tax credits, in the jurisdictions in which we operate and any adverse change to these regimes, the application thereof or challenges to the tax position we have adopted under these regimes could adversely affect our results of operations and financial condition.***

As of December 31, 2017, we had federal and state NOL carryforwards in the United States of \$7,820,000 and \$7,779,000, respectively, and cumulative carryforward tax losses in the United Kingdom of \$39,971,000, which we expect to be available to reduce future taxable income subject to any relevant restrictions (including those in the UK that limit the percentage of profits that can be reduced by carried forward losses). The U.S. federal and state NOL carry forwards will begin to expire in 2035 and the U.K. carryforward tax losses will continue indefinitely, subject to relevant restrictions, under current UK legislation. Also, as of December 31, 2017, we had research and development credits in the U.S. in the amount of \$697,000.

The NOL carry forwards and U.K. carryforward tax losses are subject to review and possible adjustment by the U.S., U.K. and state tax authorities. NOL carryforwards and U.K. carryforward tax losses may become subject to limitations in the event of certain cumulative changes in the ownership interest of significant shareholders, as defined under Sections 382 Internal Revenue Code, as well as the Corporation Tax Act 2010 Part 14 under the UK tax rules. This could limit the amount of NOLs or carryforward tax losses that we can utilize annually to offset future taxable income or tax liabilities. Subsequent ownership changes and changes to the UK (or US) tax rules in respect of the utilization of losses carried forward may further affect the limitation in future years.

Additionally, we have not undertaken a study on the completeness of the U.S. research and development credit. As such, the U.S. research and development credits may change and may be subject to review and adjustment by the tax authorities.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that can involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, future revenue, timing and likelihood of success, plans and objectives of management for future operations, future results of anticipated products and prospects, plans and objectives of management are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential,” “would” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described under the sections in this prospectus entitled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

## **INDUSTRY AND OTHER DATA**

We obtained the industry, market and competitive position data in this prospectus from our own internal estimates and research as well as from industry and general publications and research, surveys and studies conducted by third parties. Industry publications, studies and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research as to such matters is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source.

## USE OF PROCEEDS

We estimate that the net proceeds to us from our issuance and sale of our ordinary shares in this offering will be approximately \$ \_\_\_\_\_ million, assuming an initial public offering price of \$ \_\_\_\_\_ per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters' option to purchase additional shares from us is exercised in full, we estimate that our net proceeds will be approximately \$ \_\_\_\_\_ million. Each \$1.00 increase (decrease) in the assumed initial public offering price of \$ \_\_\_\_\_ per ordinary share would increase (decrease) the net proceeds to us from this offering by approximately \$ \_\_\_\_\_ million, assuming that the number of ordinary shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million in the number of ordinary shares we are offering would increase (decrease) the net proceeds to us from this offering by approximately \$ \_\_\_\_\_ million, assuming that the initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We anticipate that we will use the net proceeds of this offering for the following purposes:

- approximately \$ \_\_\_\_\_ million to further develop our most advanced product candidates, AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1;
- approximately \$ \_\_\_\_\_ million to scale up our manufacturing facility and related processes;
- approximately \$ \_\_\_\_\_ million to fund research and development of our other pipeline product candidates and technologies; and
- the remainder, if any, to fund new and ongoing research and development activities and for working capital and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. We may also use a portion of the net proceeds to in-license, acquire or invest in additional businesses, technologies, products or assets, although currently we have no specific agreements, commitments or understandings in this regard. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. Predicting the cost necessary to develop product candidates can be difficult and we anticipate that we will need additional funds to complete the development of any product candidates we identify. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from preclinical studies and any ongoing clinical trials or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Based on our planned use of the net proceeds of this offering and our current cash and cash equivalents, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements through \_\_\_\_\_. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources.

Pending our use of the net proceeds from this offering, we may invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

## **DIVIDEND POLICY**

We have never declared or paid any cash dividends on our ordinary shares. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. However, if we do pay a cash dividend on our ordinary shares in the future, we will only pay such dividend out of our profits or share premium (subject to solvency requirements) as permitted under Cayman Islands law.

## CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of March 31, 2018, as follows:

- on an actual basis;
- on a pro forma basis to reflect the corporate reorganization described under “Summary—Corporate Reorganization”; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of ordinary shares in this offering at an assumed initial public offering price of \$ per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this information in conjunction with our consolidated financial statements and the related notes appearing at the end of this prospectus and the “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section and other financial information contained in this prospectus.

	As of March 31, 2018		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
Cash and cash equivalents	\$ 32,356,851	\$	\$
Warrant liability	\$ 2,010,225	\$	\$
Series C preferred shares, \$0.00001 nominal value per share; 36,330,692 shares issued and outstanding, actual; no shares, issued and outstanding, pro forma and pro forma as adjusted	97,351,080		
Shareholders’ (deficit) equity:			
A Ordinary shares, \$0.00001 nominal value per share; 36,235,113 shares issued and outstanding, actual; shares issued and outstanding, pro forma and pro forma as adjusted	364		
Capital in excess of nominal value	23,691,708		
Accumulated other comprehensive loss	(2,780,242)		
Accumulated deficit	(81,827,196)		
Total shareholders’ (deficit) equity	(60,915,366)		
Total capitalization	\$ 36,435,714	\$	\$

- (1) Each \$1.00 increase (decrease) in the assumed initial public offering price of \$ per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, capital in excess of nominal value, total shareholders’ equity and total capitalization by \$ million, assuming that the number of ordinary shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million in the number of ordinary shares offered by us at the assumed initial public offering price per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, capital in excess of nominal value, total shareholders’ equity and total capitalization by approximately \$ million.

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The number of shares in the table above includes 144,646 unvested restricted shares and does not include:

- 6,265,500 ordinary shares issuable upon exercise of share options outstanding under our 2016 Plan as of March 31, 2018, at a weighted-average exercise price of \$1.37 per ordinary share; and
- additional ordinary shares reserved for future issuance under our 2018 Plan, which will become effective in connection with this offering, as well as any automatic increases in the number of our ordinary shares reserved for future issuance under the 2018 Plan.

## DILUTION

If you invest in our ordinary shares in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per ordinary share and the pro forma as adjusted net tangible book value per ordinary share after this offering.

As of March 31, 2018, we had a historical net tangible book value of \$36,235,113, or \$0.62 per ordinary share. Our historical net tangible book value per share represents total tangible assets less total liabilities, divided by the number of our ordinary shares outstanding as of March 31, 2018.

Our pro forma net tangible book value as of March 31, 2018 was \$            million, or \$            per ordinary share. Pro forma net tangible book value represents the amount of our total tangible assets less total liabilities, after giving effect to the corporate reorganization described under “Summary—Corporate Reorganization.” Pro forma net tangible book value per ordinary share represents our pro forma net tangible book value divided by the total number of ordinary shares outstanding as of March 31, 2018, after giving effect to the pro forma adjustment described above.

After giving further effect to receipt of the net proceeds from our issuance and the sale of            ordinary shares in this offering at an assumed initial public offering price of \$            per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2018 would have been approximately \$            million, or approximately \$            per ordinary share. This amount represents an immediate increase in pro forma net tangible book value of \$            per ordinary share to our existing shareholders and an immediate dilution of approximately \$            per ordinary share to new investors participating in this offering. We determine dilution by subtracting the pro forma as adjusted net tangible book value per ordinary share after this offering from the amount of cash that a new investor paid for an ordinary share. The following table illustrates this dilution:

Assumed initial public offering price per ordinary share	\$
Historical net tangible book value per ordinary share as of March 31, 2018	\$0.62
Increase per ordinary share attributable to the conversion of our preferred shares	_____
Pro forma net tangible book value per ordinary share as of March 31, 2018	_____
Increase per ordinary share attributable to this offering	_____
Pro forma as adjusted net tangible book value per ordinary share after this offering	_____
Dilution per ordinary share to new investors in this offering	\$ _____

Each \$1.00 increase (decrease) in the assumed initial public offering price of \$            per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per ordinary share after this offering by \$            million, and dilution in pro forma net tangible book value per ordinary share to new investors by \$           , assuming that the number of ordinary shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase of 1.0 million in the number of ordinary shares offered by us would increase our pro forma as adjusted net tangible book value per ordinary share after this offering by \$            per ordinary share and decrease the dilution to new investors by \$            per ordinary share, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us. A decrease of 1.0 million in the number of ordinary shares offered by us would decrease our pro forma as adjusted net tangible book value per ordinary share after this offering by \$            per ordinary share and increase the



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dilution to new investors by \$ \_\_\_\_\_ per ordinary share, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional ordinary shares in full, the pro forma as adjusted net tangible book value after this offering would be \$ \_\_\_\_\_ per ordinary share, the increase in pro forma net tangible book value per ordinary share would be \$ \_\_\_\_\_ and the dilution per share to new investors would be \$ \_\_\_\_\_ per ordinary share, in each case assuming an initial public offering price of \$ \_\_\_\_\_ per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us.

The following table summarizes the pro forma as adjusted basis described above, as of March 31, 2018, the differences between the number of ordinary shares purchased from us, the total consideration paid to us in cash and the average price per share that existing shareholders and new investors paid. The calculation below is based on an assumed initial public offering price of \$ \_\_\_\_\_ per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Average Price
	Number	Percent	Number	Percent	Per Share
Existing shareholders		%	\$	%	\$
New investors					
Total		100.0%		100.0%	

The foregoing tables and calculations are based on the number of our ordinary shares outstanding as of March 31, 2018 (which included 144,646 unvested restricted shares subject to repurchase), after giving effect to the automatic conversion of all preferred shares into ordinary shares in connection with this offering, and exclude:

- 6,265,500 ordinary shares issuable upon exercise of share options outstanding under our 2016 Plan as of March 31, 2018, at a weighted-average exercise price of \$1.37 per share; and
- \_\_\_\_\_ additional ordinary shares reserved for future issuance under our 2018 Plan, which will become effective in connection with this offering, as well as any automatic increases in the number of our ordinary shares reserved for future issuance under the 2018 Plan.

To the extent any of these outstanding options is exercised, there will be further dilution to new investors. If all of such outstanding options had been exercised as of March 31, 2018, the pro forma as adjusted net tangible book value per ordinary share after this offering would be \$ \_\_\_\_\_, and total dilution per ordinary share to new investors would be \$ \_\_\_\_\_.

If the underwriters exercise their option to purchase additional ordinary shares in full:

- the percentage of our ordinary shares held by existing shareholders will decrease to approximately \_\_\_\_\_ % of the total number of our ordinary shares outstanding after this offering; and
- the number of shares held by new investors will increase to \_\_\_\_\_, or approximately \_\_\_\_\_ % of the total number of our ordinary shares outstanding after this offering.

## SELECTED CONSOLIDATED FINANCIAL DATA

The following tables present our selected consolidated financial as of the dates and for the periods indicated. We have derived the consolidated statement of operations and comprehensive loss data for the years ended December 31, 2016 and 2017 from our audited consolidated financial statements appearing at the end of this prospectus. We have derived the consolidated balance sheet data as of March 31, 2018 and the consolidated statement of operations and comprehensive loss data for the three months ended March 31, 2017 and 2018 from our unaudited financial statements included elsewhere in this prospectus. These unaudited financial statements have been prepared on a basis consistent with our audited financial statements and, in our opinion, contain all adjustments, consisting of normal and recurring adjustments, necessary for the fair presentation of such financial data.

Our historical results are not necessarily indicative of the results that should be expected in any future period. You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section of this prospectus

	<u>Year Ended December 31,</u>		<u>Three Months Ended March 31,</u>	
	<u>2016</u>	<u>2017</u>	<u>2017</u>	<u>2018</u>
<b>Consolidated Statement of Operations and Comprehensive Loss Data:</b>				
Operating expenses:				
General and administrative	\$ 6,026,529	\$ 9,325,017	\$ 2,148,540	\$ 11,122,016
Research and development	14,037,918	22,359,712	4,823,357	6,927,322
Total operating expenses	<u>20,064,447</u>	<u>31,684,729</u>	<u>6,971,897</u>	<u>18,049,338</u>
Loss from operations	(20,064,447)	(31,684,729)	(6,971,897)	(18,049,338)
Other non-operating income (expense):				
Foreign currency gain	265,543	1,676,117	149,249	978,624
Convertible note inducement	—	(553,500)	—	—
Change in fair market value of warrant liability	—	(465,633)	—	669,408
Interest income	32,068	26,073	10,389	25,308
Interest expense	(25,440)	(42,863)	(8,126)	(27,355)
Net loss	<u>(19,792,276)</u>	<u>(31,044,535)</u>	<u>(6,820,385)</u>	<u>(16,403,353)</u>
Net loss attributable to non-controlling interest in subsidiary	305,883	—	—	—
Net loss attributable to MeiraGTx shareholders	<u>(19,486,393)</u>	<u>(31,044,535)</u>	<u>(6,820,385)</u>	<u>(16,403,353)</u>
Other comprehensive loss	(671,391)	(1,361,365)	(130,895)	(757,765)
Comprehensive loss	<u>(20,157,784)</u>	<u>(32,405,900)</u>	<u>(6,951,280)</u>	<u>(17,161,118)</u>
Less: comprehensive loss (income) attributable to non-controlling interest	8,520	—	—	—
Comprehensive loss attributable to MeiraGTx shareholders	<u>\$ (20,149,264)</u>	<u>\$ (32,405,900)</u>	<u>\$ (6,951,280)</u>	<u>\$ (17,161,118)</u>
Net loss attributable to MeiraGTx ordinary shareholders	<u>\$ (19,486,393)</u>	<u>\$ (31,044,535)</u>	<u>\$ (6,820,385)</u>	<u>\$ (16,403,353)</u>
Accretion on Series C preferred shares	(85,425)	(806,963)	(22,761)	(664,718)
Adjusted net loss attributable to MeiraGTx ordinary shareholders	<u>\$ (19,571,818)</u>	<u>\$ (31,851,498)</u>	<u>\$ (6,843,146)</u>	<u>\$ (17,068,071)</u>

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	<u>Year Ended December 31,</u>		<u>Three Months Ended March 31,</u>	
	<u>2016</u>	<u>2017</u>	<u>2017</u>	<u>2018</u>
Basic and diluted net loss per ordinary share attributable to ordinary shareholders(1)	<u>\$ (0.63)</u>	<u>\$ (0.96)</u>	<u>\$ (0.21)</u>	<u>\$ (0.49)</u>
Weighted-average number of ordinary shares outstanding—basic and diluted(1)	<u>31,098,591</u>	<u>33,269,157</u>	<u>32,851,408</u>	<u>34,647,368</u>

(1) See Note 12 to our consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical basic and diluted net loss per ordinary share and the weighted-average number of shares used in the computation of the per share amounts.

	<u>As of December 31,</u>		<u>As of March 31,</u>
	<u>2016</u>	<u>2017</u>	<u>2018</u>
<b>Consolidated Balance Sheet Data:</b>			
Cash and cash equivalents	\$ 17,476,641	\$ 8,548,638	\$ 32,356,851
Total assets	\$ 22,551,149	\$ 25,854,219	\$ 50,780,903
Total liabilities	\$ 6,856,572	\$ 21,880,853	\$ 14,345,189
Convertible preferred C shares	\$ 32,833,660	\$ 51,338,631	\$ 97,351,080
Total shareholders' deficit	\$ (17,139,083)	\$ (47,365,265)	\$ (60,915,366)

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*You should read the following discussion and analysis of financial condition and operating results together with the section captioned "Selected Financial Data" and our financial statements and the related notes appearing at the end of this prospectus. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, such as those set forth in the section of the prospectus captioned "Risk Factors" and elsewhere in this prospectus, our actual results may differ materially from those anticipated in these forward-looking statements. For convenience of presentation some of the numbers have been rounded in the text below.*

*MeiraGTx Holdings plc was incorporated under the laws of the Cayman Islands to become the holding company of our business pursuant to our corporate reorganization. Prior to this offering, MeiraGTx Holdings plc will have only engaged in activities incidental to its formation, the corporate reorganization and this offering. Accordingly, financial information for MeiraGTx Holdings plc and a discussion and analysis of its results of operations and financial condition for the period of its operations prior to the corporate reorganization would not be meaningful and are not presented. Following the corporate reorganization, our financial statements will present the results of operations of MeiraGTx Holdings plc and its consolidated subsidiaries.*

### Overview

We are a vertically integrated, clinical stage gene therapy company with four ongoing clinical programs and a broad pipeline of preclinical and research programs. We have core capabilities in viral vector design and optimization, gene therapy manufacturing as well as a potentially transformative gene regulation technology. Led by an experienced management team, we have taken a portfolio approach by licensing, acquiring and developing technologies that give us depth across both product candidates and indications. Though initially focusing on the eye, salivary gland and central nervous system, we intend to expand our focus in the future to develop additional gene therapy treatments for patients suffering from a range of serious diseases.

We are a private limited company incorporated under the laws of England and Wales, and were formed and commenced operations in 2015. Our discussion of our financial condition and results of operations is based upon our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. Since our formation, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facility and developing manufacturing processes, advancing the product candidates in our ophthalmology, salivary gland and neurodegenerative disease programs, building our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, and providing general and administrative support for these operations. In 2016, we completed the acquisition of assets held by BRI-Alzan, Inc., a Delaware corporation, including a worldwide license agreement to develop certain preclinical technology for the treatment of ALS. To date, we have financed our operations primarily with cash on hand and proceeds from the sales of our Series C preferred shares and Series A ordinary shares. Through March 31, 2018, we received gross proceeds of approximately \$97.6 million from sales of our Series C preferred shares. In addition, from April 1, 2018 through April 30, 2018, we issued 4,706,495 Series C preferred shares for gross proceeds of \$12.7 million. As of March 31, 2018, we had cash and cash equivalents of \$32.4 million.

We are a clinical stage company and have not generated any product revenues to date. We have four clinical programs and a pipeline of preclinical programs. Since inception, we have incurred significant operating losses. Our net losses for the three months ended March 31, 2017 and 2018 were \$6.8 million and \$16.4 million, respectively, and for the years ended December 31, 2016 and 2017 were \$19.5 million and \$31.1 million, respectively. As of March 31, 2018, we had an accumulated deficit of \$81.8 million. We do not expect to generate revenue from sales of any products for several years, if at all.

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Our total operating expenses were \$7.0 million and \$18.0 million for the three months ended March 31, 2017 and 2018, respectively, and were \$20.1 million and \$31.7 million for the years ended December 31, 2016 and 2017, respectively. We expect our operating expenses to increase substantially in connection with our ongoing development activities related to our product candidates. We anticipate that our expenses will increase due to costs associated with our clinical development program targeting in achromatopsia due to mutations in the *CNGB3* or *CNGA3* gene, inherited retinal dystrophy caused by mutations in *RPE65*, or *RPE65*-deficiency, and X-Linked retinitis pigmentosa, or XLRP. In addition, we expect to incur increasing costs associated with our clinical activities for *hAQP1* for the treatment of radiation-induced xerostomia. We also expect to incur expenses related to research activities in additional therapeutic areas to expand our pipeline, hiring additional personnel in manufacturing, research, clinical trials, quality and other functional areas, and associated cash and share-based compensation expense, as well as the further development of internal manufacturing capabilities and capacity and other associated costs including the management of our intellectual property portfolio. In addition, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company.

As a result of these anticipated expenditures, we will require additional capital beyond the proceeds of this offering, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable us to complete the development and potential commercialization of our product candidates. Furthermore, upon closing of this offering, we expect to incur additional costs associated with being a public company. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our product candidate development efforts. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate certain of our research and development programs.

We expect that our existing cash and cash equivalents, together with anticipated net proceeds from this offering, will enable us to fund our current and planned operating expenses and capital expenditures for at least the next months. We have based these estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. See “—Liquidity and Capital Resources.” Because of the numerous risks and uncertainties associated with the development of our product candidates, any future product candidates, our platform and technology and because the extent to which we may enter into collaborations with third parties for development of any of our product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

- the initiation, progress, timing, costs and results of our planned clinical trials for our product candidates;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, EMA and other regulatory authorities;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or any of our product candidates;
- the effect of competing technological and market developments;
- the costs and timing of further developing our manufacturing facilities in the United Kingdom;
- the costs of operating as a public company.

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- the extent to which we in-license or acquire other products and technologies;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates in regions where we choose to commercialize our products; and
- the initiation, progress, timing and results of our commercialization of our product candidates, if approved for commercial sale.

Adequate additional funds may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. Any future debt financing or preferred equity or other financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute your ownership interests.

If we raise additional funds through collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

### **Components of Our Results of Operations**

#### ***Operating Expenses***

Our operating expenses since inception have consisted primarily of general and administrative costs and research and development costs.

#### ***General and Administrative Expenses***

General and administrative expenses consist primarily of salaries and other related costs, including share-based compensation, for personnel in our executive, finance, business development and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and office facility-related expenses, which include direct depreciation costs.

We expect that our general and administrative expenses will increase in the future as we increase our personnel headcount to support increased research and development activities. We also expect to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with Nasdaq and SEC requirements; director and officer insurance costs; and investor and public relations costs.

### Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, and include:

- employee-related expenses, including salaries, benefits and travel of our research and development personnel;
- expenses incurred in connection with third-party vendors that conduct clinical and preclinical studies and manufacture the drug product for the clinical trials and preclinical activities;
- acquisition of in-process research and development;
- costs associated with clinical and preclinical activities including costs related to facilities, supplies, rent, insurance, certain legal fees, share-based compensation, and depreciation; and
- expenses incurred with the development and operation of our manufacturing facility.

We expense research and development costs as incurred.

We typically use our employee and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, license payments made under our licensing arrangements or other internal costs to specific development programs or product candidates. These costs are included in other research and development expenses in the table below.

The following table summarizes our research and development expenses:

	Year Ended December 31,			Three Months Ended March 31,		
	2016	2017	Change	2017	2018	Change
Ophthalmology programs	\$ 2,026,592	\$ 4,133,015	\$2,106,423	\$ 766,505	\$1,465,179	\$ 698,674
Salivary gland programs	967,745	913,706	(54,039)	225,101	211,215	(13,886)
Neurodegenerative diseases programs	922,127	2,220,843	1,298,716	425,737	604,518	178,781
Manufacturing	379,656	3,213,861	2,834,205	275,868	792,387	516,519
Other research and development costs	9,741,798	11,878,287	2,136,489	3,130,144	3,854,023	723,879
Total research and development expenses	<u>\$14,037,918</u>	<u>\$22,359,712</u>	<u>\$8,321,794</u>	<u>\$4,823,355</u>	<u>\$6,927,322</u>	<u>\$2,103,967</u>

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase substantially for the foreseeable future as we initiate additional preclinical and clinical trials of our existing product candidates and continue to discover and develop additional product candidates.

We cannot determine with certainty the duration and costs of future clinical trials of our product candidates or any other product candidate we may develop or if, when, or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any product candidate. The duration, costs and

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timing of clinical trials and development of our existing product candidates or any other product candidate we may develop will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of clinical trials of our existing product candidates, as well as of any future clinical trials of other product candidates and other research and development activities that we may conduct;
- uncertainties in clinical trial design and patient enrollment rates;
- the actual probability of success for our product candidates, including the safety and efficacy, early clinical data, competition, manufacturing capability and commercial viability;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any marketing approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another U.S. or foreign regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

### ***Other non-operating income (expense)***

Other non-operating income (expense) includes the following:

#### *Foreign currency gain*

Our consolidated financial statements are presented in U.S. dollars, which is our reporting currency. The financial position and results of operations of our subsidiaries MeiraGTx UK II and MeiraGTx B.V. are measured using the foreign subsidiaries' local currency as the functional currency. MeiraGTx UK II cash accounts holding U.S. dollars are remeasured based upon the exchange rate at the date of remeasurement with the resulting gain or loss included in the consolidated statement of operations and comprehensive loss. Expenses of such subsidiaries have been translated into U.S. dollars at average exchange rates prevailing during the period. Assets and liabilities have been translated at the rates of exchange on the consolidated balance sheet date. The resulting translation gain and loss adjustments are recorded directly as a separate component of shareholders' equity and as other comprehensive loss on the consolidated statement of operations and comprehensive loss.

#### *Convertible note inducement expense*

Convertible note inducement expense consists of the issuance of a warrant to a convertible note holder as an inducement to convert the note payable into Series C preferred shares.

#### *Change in fair value of warrant liability*

We have determined that our warrants are classified as liabilities on our balance sheet because the Series C preferred shares underlying the warrants have a redemption feature in the event of a change of control of the



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Company. The fair values of the warrants are estimated using the Black-Scholes valuation model with certain assumptions regarding risk free interest rate, expected volatility, expected divided yield and expected life. The Black-Scholes value of the warrants was recorded as a warrant liability and is remeasured quarterly. Any changes in the quarterly valuation of the warrants is charged to operations.

### **Critical Accounting Policies and Use of Estimates**

Our management's discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of our financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing at the end of this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

### **Consolidation**

Our consolidated financial statements include the accounts of MeiraGTx Limited and its wholly owned subsidiaries, MeiraGTx, LLC, a Delaware limited liability company, BRI-Alzan, Inc., a Delaware corporation, (the assets of which we acquired in 2016, as described above), MeiraGTx B.V., a Netherlands corporation, and MeiraGTx UK Limited, a limited company incorporated under the laws of England and Wales. The consolidated financial statements also include the accounts of MeiraGTx UK II Limited, a limited company incorporated under the laws of England and Wales, which was a 60% owned subsidiary from April 27, 2015 through April 8, 2016. On April 8, 2016, we acquired the remaining 40% of interest in MeiraGTx UK II Limited.

All intercompany balances and transactions between the consolidated companies have been eliminated in consolidation.

### **Foreign Currencies**

Our consolidated financial statements are presented in U.S. dollars, our reporting currency. The financial position and results of operations of MeiraGTx UK II and MeiraGTx UK II cash accounts holding U.S. dollars are remeasuring based upon the exchange rate at the date of remeasurement with the resulting gain or loss included in the consolidated statement of operations and comprehensive loss. Expenses of such subsidiaries have been translated into U.S. dollars at average exchange rates prevailing during the period. Assets and liabilities have been translated at the rates of exchange on the consolidated balance sheet dates. The resulting translation gain and loss adjustments are recording directly as a separate component of shareholders' equity and as other comprehensive loss on the consolidated statements of operations and comprehensive loss.

### **Income Taxes**

Since our inception in 2015, we have not recorded any U.K. or U.S. federal or state income tax benefits for the net losses we have incurred in any year or for our U.S. research and development tax credits, due to our uncertainty of realizing a benefit from those items. As of December 31, 2017, we had U.S. federal and state net operating loss carryforwards of \$7.8 million and \$7.8 million, respectively, each of which begin to expire in 2035. We also had U.K. net operating loss carryforwards of \$40.0 million, which will continue indefinitely under current U.K. legislation.

### ***Research and Development***

Research and development costs are charged to expense as incurred. These costs include, but are not limited to, employee-related expenses, including salaries, benefits and travel of our research and development personnel; expenses incurred under agreements with contract research organizations and investigative sites that conduct clinical and preclinical studies and manufacture the drug product for the clinical studies and preclinical activities; acquisition of in-process research and development; facilities; supplies; rent, insurance, certain legal fees, stock-based compensation, depreciation and other costs associated with clinical and preclinical activities and regulatory operations. Refundable research and development tax credits received are recorded as an offset to these costs.

Costs for certain development activities, such as outside research programs funded by us, are recognized based on an evaluation of the progress to completion of specific tasks with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.

### ***Share-Based Compensation***

#### *Options*

We grant share options to employees, non-employee members of our board of directors and non-employee consultants as compensation for services performed. Employee and non-employee members of the board of directors' awards of share-based compensation are accounted for in accordance with ASC 718, Compensation—Stock Compensation, or ASC 718. ASC 718 requires all share-based payments to employees and non-employee directors, including grants of share options, to be recognized in the statement of operations and comprehensive loss based on their grant date fair values. The grant date fair value of share options is estimated using the Black-Scholes option valuation model.

Using this model, fair value is calculated based on assumptions with respect to (i) the fair value our ordinary shares on the grant date; (ii) expected volatility of our ordinary share price, (iii) the periods of time over which employees and members of our board of directors are expected to hold their options prior to exercise (expected term), (iv) expected dividend yield on our ordinary shares, and (v) risk-free interest rates.

Our ordinary shares have not been traded on a public exchange. Therefore, we do not have sufficient company-specific information available to determine the expected term based on its historical data. As a result, the expected term of share options granted to employees and members of our board of directors is determined using the average of the vesting period and contractual life of the option, an accepted method for our option grants under the SEC's Staff Accounting Bulletin No. 107 and No. 110, Share-Based Payment.

Similarly, we believe that our future volatility will differ materially during the expected term from the volatility that would be calculated from our historical share prices to date. Consequently, expected volatility is based on an analysis of guideline companies in accordance with ASC 718. The expected dividend yield is zero as we have never paid dividends and do not currently anticipate paying any in the foreseeable future. Risk-free interest rates are based on quoted U.S. Treasury rates for securities with maturities approximating the option's expected term.

As of January 1, 2016, we early adopted ASU 2016-09, Improvements to Employee Share-Based Payment Accounting, and accounts for forfeitures as they occur from that date. Additionally, excess tax benefits and deficiencies will be recognized as income tax expense or benefit in the income statement. There was no cumulative effect adjustment as we did not issue any options prior to January 1, 2016.

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We account for options granted to non-employee consultants under ASC 505-50, Equity-Based Payments to Non-Employees. As such, we estimate the fair value of each such option using the Black-Scholes model, with the expected term of share options granted to non-employees initially equal to the options' maximum contractual life of ten years, at issuance. On each subsequent reporting date until performance is complete, we revalue all outstanding options granted to non-employee consultants during the vesting period of each tranche. Under ASC 505-50, upon re-measurement of each award, income or expense is recognized during its vesting term. Compensation cost relating to awards with service-based graded vesting schedules is recognized as general and administrative and research and development expenses in the consolidated statement of operations and comprehensive loss using the straight-line method.

### *Restricted Shares*

In connection with certain service agreements and research agreements, we have granted restricted Ordinary Shares as compensation. The shares are recognized in the statement of operations and comprehensive loss based on their grant date fair values. Compensation cost relating to share grants with service-based graded vesting schedules is recognized based on the vesting schedule.

### ***Determination of Fair Value of Ordinary Shares***

As there has been no public market for our ordinary shares to date, the estimated fair value of our ordinary shares has been determined by our board of directors as of the date of each option grant, with input from management, considering our most recently available third-party valuations of ordinary shares and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant.

Third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. The third party estimated the fair value of the equity value of our company using a special case of the market approach known as the backsolve method. The backsolve method was used to solve for the implied total equity value based on our issuances of Series C preferred shares. Consideration was given to the rights and preferences of each of our classes of equity and the expected time to a liquidity event. An option pricing allocation method, or OPM, was selected to allocate the total equity value. The OPM treats ordinary shares and preferred shares as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the ordinary shares have value only if the funds available for distribution to shareholders exceeded the value of the preferred share liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. These third-party valuations resulted in a valuation of our ordinary shares of \$1.95, \$0.68, \$1.45 and \$1.55 per share as of December 31, 2016, September 15, 2017, December 31, 2017 and March 31, 2018, respectively.

The decrease in the valuation from December 31, 2016 to September 15, 2017 was due primarily to the Company decreasing the offering price of the Series C preferred shares from \$5.40 per share at December 31, 2016 to \$2.70 per share at September 15, 2017. Additionally, warrants were issued in connection with the issuance of Series C preferred shares at that time.

In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our ordinary shares as of each grant date, including:

- the prices at which we sold Series C preferred shares and the superior rights and preferences of the Series C preferred shares relative to our ordinary shares at the time of each grant;
- the progress of our research and development programs, including the status and results of clinical trials and preclinical studies for our product candidates;

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- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our ordinary shares and our Series C preferred shares;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used different assumptions or estimates, the fair value of our ordinary shares and our share-based compensation expense could have been materially different.

### ***Warrant Liability***

During 2017, we issued warrants to purchase Series C preferred shares to certain investors. Due to the potential redemption feature of the underlying Series C preferred shares, the warrants have been classified as a liability. Liability accounting requires that the fair value of warrants be remeasured each reporting period with changes recorded in the statement of operations and comprehensive loss. These warrants to purchase Series C preferred shares will remain outstanding until the exercise or expiration of the warrants or the completion of this offering, at which time the warrant liability will be remeasured to fair value and reclassified to capital in excess of nominal value.

For the unobservable inputs for the warrants, the expected volatility was determined at each measurement date by taking an average of the volatility of other publicly traded peer biotechnology companies.

The expected life was determined at each measurement date based upon our estimate of the time until the Company has a conversion event, as described in Note 11 of our consolidated financial statements included elsewhere in this prospectus. The fair value of the Series C preferred shares were based upon recent issuances of our Series C preferred shares on or about these dates.

The estimated fair values of our warrants are not necessarily indicative of the amounts that would be realized in a current market exchange. The determination of the fair value of the warrants are sensitive to changes in in the assumptions used and a change in those inputs could result in a significantly higher or lower fair value measurement. If the volatility were to increase or the expected life were to increase, the fair value of the warrants would increase. Conversely, if the volatility were to decrease or the expected life were to decrease, the fair value of the warrants would decrease.

### ***Series C preferred shares***

The Series C preferred shares are not redeemable. However in the event of a Sale (as defined in the Articles of Association), which would include a change of control that is outside of our control, the Series C preferred shares are entitled to receive a payment which is equal to their liquidation value. The feature is being accounted for as a redemption under ASC 480.

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We are accounting for our Series C preferred shares under the requirements of ASC 480 which establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. The carrying value of the Series C preferred shares is presented in as temporary equity and is increased by periodic accretions so that the carrying amount will equal the redemption amount at the estimated date that the Series C preferred shares will be converted into ordinary shares. These increases are affected through charges against additional paid-in capital, to the extent it is available, or accumulated deficit. For all issuances of Series C preferred shares, the difference between the amount invested by the holders of the Series C preferred shares, net of issuance costs and the initial fair value of warrants issued in connection with the Series C preferred shares (if applicable) and the liquidation value of the Series C preferred shares is recorded as accretion over the estimated life of the Series C preferred shares. The accretion is added to net loss to arrive at the net loss available to ordinary shareholders in the calculation of loss per ordinary share.

### Results of Operations

#### Comparison of Three Months Ended March 31, 2017 and 2018

The following table summarizes our results of operations for the three months ended March 31, 2017 and 2018, respectively:

	Three Months Ended March 31,		
	2017	2018	Change
Operating expenses:			
General and administrative	\$ 2,148,540	\$ 11,122,016	\$ 8,973,476
Research and development	4,823,357	6,927,322	2,103,965
Total operating expenses	6,971,897	18,049,338	11,077,441
Loss from operations	(6,971,897)	(18,049,338)	(11,077,441)
Other non-operating income (expense):			
Foreign currency gain	149,249	978,624	829,375
Change in fair value of warrant liability	—	669,408	669,408
Interest income	10,389	25,308	14,919
Interest expense	( 8,126)	(27,355)	( 19,229)
Net loss	<u><u>\$ (6,820,385)</u></u>	<u><u>\$ (16,403,353)</u></u>	<u><u>\$ ( 9,582,968)</u></u>

#### General and Administrative Expenses

General and administrative expenses were \$2.1 million for the three months ended March 31, 2017, compared to \$11.1 million for the three months ended March 31, 2018. The increase of \$9.0 million was primarily due to increases of \$5.8 million in payroll, \$3.3 million in stock-based compensation, \$0.1 million in consultant costs, \$0.1 million in legal and \$0.2 million in accounting fees, which was partially offset by decreases of \$0.4 million in rent and \$0.1 million in depreciation expenses.

#### Research and Development Expenses

Research and development expenses for the three months ended March 31, 2017 were \$4.8 million, compared to \$6.9 million for the three months ended March 31, 2018. The increase of \$2.1 million was primarily due to an increase in costs of \$1.8 million related to preparation for production of our manufacturing facility, \$0.2 million in license fees and \$0.1 million in neurodegenerative research.

#### Foreign Currency Gain

Foreign currency gain was \$0.1 million for the three months ended March 31, 2017 compared to \$1.0 million for the three months ended March 31, 2018. The increase of \$0.8 million was primarily due to a weakening U.S. dollar against the pound sterling during the three months ended March 31, 2018.

### *Change in Fair Market Value of Warrant Liability*

The change in fair market value of the warrant liability for the three months ended March 31, 2018 was due to the revaluation of warrants, which were issued to certain investors in September and November 2017, using the Black-Scholes valuation model at December 31, 2017 and March 31, 2018. As a result of the revaluation, there was a decrease of \$0.7 million in the fair market value of the warrant liability at March 31, 2018, which resulted in a gain being recorded for the three months ended March 31, 2018.

### *Comparison of Years Ended December 31, 2016 and 2017*

The following table summarizes our results of operations for the years ended December 31, 2016 and 2017, respectively:

	2016	Year Ended December 31, 2017	Change
Operating expenses:			
General and administrative	\$ 6,026,529	\$ 9,325,017	\$ 3,298,488
Research and development	14,037,918	22,359,712	8,321,794
Total operating expenses	20,064,447	31,684,729	11,620,282
Loss from operations	(20,064,447)	(31,684,729)	(11,620,282)
Other non-operating income (expense):			
Foreign currency gain	265,543	1,676,117	1,410,574
Convertible note inducement expense	—	(553,500)	(553,500)
Change in fair value of warrant liability	—	(465,633)	(465,633)
Interest income	32,068	26,073	(5,995)
Interest expense	(25,440)	(42,863)	(17,423)
Net loss	<u>\$ (19,792,276)</u>	<u>\$ (31,044,535)</u>	<u>\$ (11,252,259)</u>

#### *General and Administrative Expenses*

General and administrative expenses were \$6.0 million for the year ended December 31, 2016, compared to \$9.3 million for the year ended December 31, 2017. The increase of \$3.3 million was primarily due to increases of \$0.8 million in payroll, \$0.5 million in legal, \$1.7 million in rent and \$0.3 million in depreciation expenses.

#### *Research and Development Expenses*

Research and development expenses for the year ended December 31, 2016 were \$14.0 million, compared to \$22.4 million for the year ended December 31, 2017. The increase of \$8.4 million was primarily due to an increase in costs of \$2.5 million related to preparation for production of our manufacturing facility, \$0.9 million related costs of consultants, \$5.1 million of clinical trial costs related to our ophthalmology programs, \$0.8 million in payroll, \$1.0 million in neurodegenerative research, and \$0.4 million in share-based compensation which was partially offset by a decrease of \$0.6 million in acquired research and development related to an asset acquisition in 2016 and the receipt of a \$1.7 million research and development credit in the United Kingdom in 2017.

#### *Foreign Currency Gain*

Foreign currency gain was \$0.3 million for the year ended December 31, 2016 compared to \$1.7 million for the year ended December 31, 2017. The increase of \$1.4 million was primarily due to a weakening U.S. dollar against the pound sterling in 2017.

*Convertible Note Inducement Expense*

There was no convertible note inducement expense for the year ended December 31, 2016 compared to \$0.5 million for the year ended December 31, 2017. The increase of \$0.5 million was primarily due to the issuance of a warrant to purchase 900,000 Series C preferred shares in 2017 to a convertible noteholder as an inducement to convert the note into Series C preferred shares.

*Change in Fair Market Value of Warrant Liability*

There was no warrant liability for the year ended December 31, 2016, compared to \$0.5 million for the year ended December 31, 2017. The increase of \$0.5 million was primarily due to the revaluation of certain warrants, which were issued to certain investors in September and November 2017, using the Black-Scholes valuation model at December 31, 2017.

***Liquidity and Capital Resources***

Since our inception, we have incurred significant operating losses. We have not generated positive cash flows from operations, and there are no assurances that we will be successful in obtaining an adequate level of financing for the development and commercialization of its product candidates. These factors raise substantial doubt about our ability to continue as a going concern. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and clinical development of our product candidates. We expect that our research and development and general and administrative costs will increase in connection with conducting preclinical studies and clinical trials for our product candidates, building out internal capacity to have product manufactured to support preclinical studies and clinical trials, expanding our intellectual property portfolio, and providing general and administrative support for our operations. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements, or other sources.

We are required to maintain a stand-by letter of credit as a security deposit under a certain lease with ARE, an entity that is under common control with an entity that is a minority shareholder of the Company and whose CEO is on our board of directors. See “Certain Relationships and Related Person Transactions.” Our bank requires us to maintain restricted cash balances to serve as collateral for the letter of credit issued to the landlord by the bank. In connection with an amendment to one of the ARE leases in November 2017, one of the letters of credit in the amount of \$321,978 and the related restricted cash balance were released in December 2017. As of December 31, 2016 and 2017, the restricted cash balances for the ARE leases were invested in a commercial money market account. The restricted cash balance for the other ARE lease remains at \$123,376 through the end of the lease term in December 2021, plus three months. We had \$444,844 and \$123,376 of restricted cash included in long-term assets as of December 31, 2016 and 2017, respectively, and \$444,844 and \$123,376 of restricted cash included in long-term assets as of March 31, 2017 and 2018, respectively.

We do not currently have any approved products and have never generated any revenue from product sales. To date, we have financed our operations primarily through the sale of our Series C preferred shares and cash on hand.

## Cash Flows

As of March 31, 2018, we had \$32.4 million of cash and cash equivalents.

The following table summarizes our sources and uses of cash for the period presented:

	Year Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
Net cash used in operating activities	\$ (14,367,952)	\$ (18,055,386)	\$ (6,395,338)	\$ (17,395,969)
Net cash used in investing activities	(2,593,584)	(10,535,717)	(1,737,520)	(1,210,452)
Net cash provided by financing activities	20,757,202	19,340,215	196,543	42,401,814
Increase (decrease) in cash	\$ 3,795,666	\$ (9,250,888)	\$ (7,936,315)	\$ 23,795,393

### Operating Activities

During the three months ended March 31, 2017, our cash used in operating activities of \$6.4 million was primarily due to our net loss of \$6.8 million as we incurred expenses associated with research activities on our clinical programs and research activities for our other product candidates and incurred general and administrative expenses. The loss included non-cash charges of \$0.9 million, which consisted of \$0.9 million of share-based compensation and depreciation of \$0.2 million, which was partially offset by a foreign currency gain of \$0.2 million. Additionally, current assets, consisting of prepaid expenses and other current assets, increased by \$0.5 million.

During the three months ended March 31, 2018, our cash used in operating activities of \$17.4 million was primarily due to our net loss of \$16.4 million as we incurred expenses associated with research activities on our clinical programs and research activities for our other product candidates and incurred general and administrative expenses. The loss included non-cash charges of \$3.2 million, which consisted of \$4.3 million of share-based compensation, depreciation of \$0.5 million and issuance of Series C preferred shares in connection with a license agreement of \$0.1 million, which was partially offset by a foreign currency gain of \$1.0 million and a change in the fair value of the warrant liability of \$0.7 million. Additionally, current liabilities, consisting of accounts payable, accrued expenses, deferred rent and due to affiliate, increased by \$4.2 million.

During the year ended December 31, 2016, our cash used in operating activities of \$14.4 million was primarily due to our net loss of \$19.8 million as we incurred expenses associated with research activities on our clinical programs and research activities for our other product candidates and incurred general and administrative expenses. The loss included non-cash charges of \$3.9 million, which consisted of \$2.8 million of share-based compensation, acquired research and development of \$0.6 million, issuance of shares for services of \$0.3 million and depreciation of \$0.2 million. Additionally, current liabilities, consisting of accounts payable, accrued expenses deferred rent and due to affiliate, increased by \$2.8 million, which was partially offset by increases in current assets, consisting of prepaid expenses and other current assets, in the amount of \$1.3 million.

During the year ended December 31, 2017, our cash used in operating activities of \$18.1 million was primarily due to our net loss of \$31.0 million as we incurred expenses associated with research activities on our clinical programs and research activities for our other product candidates and incurred general and administrative expenses. The loss included non-cash charges of \$3.0 million, which consisted of \$3.0 million of share-based compensation, change in fair value of warrant liability in the amount of \$0.5 million, convertible note inducement expense of \$0.5 million and depreciation of \$0.7 million, which was partially offset by a foreign currency gain of \$1.7 million. Additionally, current liabilities, consisting of accounts payable, accrued expenses



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deferred rent and due to affiliate, increased by \$11.1 million, was partially offset by decreases in current assets, consisting of prepaid expenses and other current assets, in the amount of \$1.2 million.

### *Investing Activities*

Net cash used in investing activities for the three months ended March 31, 2017 and March 31, 2018 of \$1.7 million and \$1.2 million, respectively, consisted of purchases of property and equipment, primarily for our manufacturing facility.

Net cash used in investing activities for the year ended December 31, 2016 and December 31, 2017 of \$2.6 million and \$10.5 million, respectively, consisted of purchases of property and equipment, primarily for our manufacturing facility.

### *Financing Activities*

Net cash provided by financing activities was \$0.2 million for the three months ended March 31, 2017, represented proceeds from the issuance of our Series C preferred shares.

Net cash provided by financing activities was \$42.4 million for the three months ended March 31, 2018, represented proceeds of \$43.8 million from the issuance of Series C preferred shares, which was partially offset by the payment of a note in the amount of \$1.4 million.

Net cash provided by financing activities was \$20.8 million for the year ended December 31, 2016, represented proceeds from the issuance of our Series C preferred shares.

Net cash provided by financing activities was \$19.3 million for the year ended December 31, 2017, represented proceeds of \$16.8 million from the issuance of Series C preferred shares and \$2.5 million from the issuance of a note payable.

### *Funding Requirements*

Our operating expenses increased substantially in 2017 and are expected to increase substantially in the future in connection with our ongoing activities, particularly as we advance our clinical activities including scale-up of manufacturing processes and additional clinical trials. In addition, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company.

Specifically, our expenses will increase as we:

- pursue the preclinical and clinical development of our product candidates;
- scale up our manufacturing processes and capabilities to support our preclinical studies and clinical trials of our product candidates;
- in-license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel in research, manufacturing and regulatory and clinical development as well as management personnel; and
- expand our operational, financial and management systems and increase personnel, including personnel to support our operations as a public company.

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We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements for at least the next months. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with research, development and commercialization of gene therapies, it is difficult to estimate with certainty the amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the progress, costs and results of our preclinical development and initial clinical trials for our gene therapy programs;
- the progress, costs and results of our additional clinical, research and preclinical development programs in gene therapy;
- the costs and timing of process development and manufacturing scale-up activities associated with our clinical programs;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;
- the scope, progress, results and costs of any product candidates that we may derive from our platform technology or any other product candidates that we may develop;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements and marketing and distribution arrangements.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of ordinary shares. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

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### Contractual Obligations and Commitments

The following is a summary of our significant contractual obligations as of December 31, 2017.

Contractual Obligation	Total	Payments Due by Period			
		Less Than 1 Year	More Than 1 Year and Less Than 3	More Than 3 years and Less Than 5	More Than 5 years
Operating lease obligation(1)	\$3,490,362	\$1,215,723	\$1,676,375	\$ 598,264	\$ —
Capitalized, lease obligations(2)	70,304	34,410	35,894	—	—
Notes payable(3)	1,527,147	1,527,147	—	—	—
Total	<u>\$5,087,813</u>	<u>\$2,777,280</u>	<u>\$1,712,269</u>	<u>\$ 598,264</u>	<u>\$ —</u>

(1) Represents the leases for office, laboratory, and manufacturing space in London, UK and New York, New York under non-cancelable operating leases that expire between July 2017 and December 2021. The lease for manufacturing space includes a 5-year option that, if exercised, would extend the expiration of that lease through February 2026. The obligation for such extension is not included in the above table.

(2) Represents future payments under capitalized leases for office equipment.

(3) Represents our note payable to ARE East-River Science Park LLC that bears interest at an annual rates of 5.0% and is due on December 31, 2018. The balance includes interest payment obligations.

The contractual obligations table does not include any potential future payments we may be required to make under (1) our license agreements with UCL Business, plc, Brandeis University and other entities or (2) our sponsored research agreements with universities and commercial research organizations. These agreements may be terminated upon 30-90 days written notice and, therefore, the amounts to be paid by us are not fixed or determinable at this time.

### Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements under applicable SEC rules and do not have any holdings in variable interest entities.

### Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities and foreign currency exchange rates. However, relative to foreign currency exposures as of December 31, 2017, a 10% unfavorable movement in foreign currency exchange rates would not expose us to a significant increase in net loss. We had cash and cash equivalents of \$17.5 million and \$8.5 million as of December 31, 2016 and 2017, respectively, which consist of bank deposits and money market funds. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant for us. Other than accounts payable and accrued expenses incurred in the ordinary course of business, we had other debt outstanding of \$0 million as of December 31, 2016, and a note payable of \$1.4 million as of December 31, 2017.

### Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an “emerging growth company,” which we are, to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

## BUSINESS

### Overview

We are a vertically integrated, clinical stage gene therapy company with four ongoing clinical programs and a broad pipeline of preclinical and research programs. We have core capabilities in viral vector design and optimization and gene therapy manufacturing, as well as a potentially transformative gene regulation technology. Led by an experienced management team, we have taken a portfolio approach by licensing, acquiring and developing technologies that give us depth across both product candidates and indications. Though initially focusing on the eye, salivary gland and central nervous system, we intend to expand our focus in the future to develop additional gene therapy treatments for patients suffering from a range of serious diseases.

We operate a flexible and scalable viral vector manufacturing facility that we expect can supply our current clinical and preclinical programs through regulatory approval and, should they be approved, provide sufficient capacity for commercial production. Completed in early 2018 and designed to meet global regulatory requirements, including the current good manufacturing practices, or cGMP, required by the U.S. Food and Drug Administration, or FDA, our 29,000 square foot facility has two cell production suites, three independent viral vector production suites providing multi-product and multi-viral vector manufacturing capabilities and an integrated, flexible fill-and-finish suite.

We have also established a comprehensive platform for the efficient clinical development of the next generation of gene therapies and manufacturing in accordance with cGMP. Our deep understanding of disease models informs our development of potency assays for the cGMP production of our product candidates, and our teams experienced in viral vector design and optimization work closely with our process development team to design viral vectors and develop proprietary production cell lines for efficient scaling of manufacturing processes.

We are also developing a potentially transformative technology to enable the use of small molecules to turn gene therapy product candidates on and off. The aim of this gene regulation platform is to convert gene therapy into a generalizable delivery mechanism for biologic drugs using a small molecule “switch” for temporal control. We believe the capacity for temporal control of gene therapy products has the potential to transform the gene therapy landscape by opening up new treatment possibilities.

### Our Pipeline

Our initial focus is on three distinct areas of unmet medical need: inherited retinal diseases, or IRDs, severe forms of xerostomia and neurodegenerative diseases. Utilizing our product development platform, we have assembled a pipeline of gene therapies to treat these serious diseases. Our criteria for selecting our initial product candidates included:

- unmet medical need;
- high potential for meaningful clinical benefit;
- promising preclinical data using multiple animal models as well as human stem cell derived organoids;
- compartmentalized anatomy of target tissue and the partially immune protected nature of target tissue; and
- understanding of the disease state from natural history studies and detailed long-term characterization of patients prior to entry into gene therapy treatment studies.

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A summary of our product candidates is below. We retain worldwide development and commercialization rights to all of our product candidates.

Product Candidate	Indication	Development Stage			Status
		Preclinical	Phase 1/2	Phase 3	
<b>Ophthalmology Programs</b>					
AAV-CNGB3	<b>Achromatopsia</b> ( <i>CNGB3</i> )	Orphan U.S. & EU; RPDD; PRIME <sup>(1,2,3,4)</sup>			• Phase 1/2 ongoing in UK <sup>(5)</sup>
AAV-CNGA3	<b>Achromatopsia</b> ( <i>CNGA3</i> )				• Phase 1/2 expected initiation in 2019
AAV-RPGR	<b>X-linked RP</b> ( <i>RPGR</i> )	Orphan U.S. & EU; Fast Track Designation <sup>(1,2,6)</sup>			• Phase 1/2 ongoing
AAV-RPE65	<b>RPE65-Deficiency</b> ( <i>RPE65</i> )	Orphan U.S. & EU; RPDD <sup>(1,2,3)</sup>			• Phase 1/2 ongoing
AAV-AIPL1	<b>LCA4</b> ( <i>AIPL1</i> )	Compassionate Use Orphan U.S. & EU <sup>(1,2)</sup>			• UK Specials License <sup>(7)</sup> approved October 2017
A006	<b>Wet AMD</b> ( <i>anti-VEGFR2</i> )				• First in man clinical trials expected 2019
<b>Salivary Gland Programs</b>					
AAV-AQP1	<b>Xerostomia</b> ( <i>hAQP1</i> )	Orphan U.S. <sup>(1)</sup>			• Phase 1 ongoing
AAV-AQP1	<b>Sjogren's</b> ( <i>hAQP1</i> )				• Phase 1/2 expected initiation in 2019
<b>Neurodegenerative Diseases Program</b>					
AAV-UPF1	<b>ALS</b> ( <i>UPF1</i> )				• First in man clinical trials expected 2019

1. Orphan drug designation by the FDA.
2. Orphan drug designation by European Medicines Agency, or the EMA.
3. Rare pediatric disease designation by Offices of Orphan Products Development and Pediatric Therapeutics of the FDA.
4. Priority medicines, or PRIME, designation by the EMA.
5. The IND for AAV-CNGB3 has not been opened yet because the FDA had a question about our device compatibility assay, placing the IND on clinical hold until the question has been satisfactorily answered.
6. Fast Track designation by the FDA.
7. Manufactured under a specials license and released for compassionate use in the United Kingdom, or UK.

In addition to these clinical and preclinical programs, we have preclinical and research programs in other indications and novel molecular technologies that we aim to advance into clinical development, including:

- neovascular age related macular degeneration, or wet AMD – use of a gene therapy product to deliver an antibody targeting the vascular endothelial growth factor receptor 2, or anti-VEGFR2, with the aim of blocking disease related vascular formation in the eye;

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- geographic atrophy age related macular degeneration, or dry AMD – use of gene therapy technology to introduce light sensitive molecules into rod photoreceptors in order to restore some aspects of vision lost in this disease;
- amyotrophic lateral sclerosis, or ALS—targeting dysregulation of neuronal RNA processing, which we believe may lead to the degeneration of motor neurons that occurs in ALS;
- Alzheimer’s disease—targeting endosomal trafficking, which is a central mechanism that we believe underlies Alzheimer’s disease; and
- gene regulation—use of our proprietary RNA shape regulation cassette to switch gene therapy product candidates on and off with small molecules, potentially transforming gene therapy technology into a delivery mechanism for a broad array of biologic drugs.

### ***Our Ophthalmology Programs***

Eye diseases are our first area of clinical focus and we aim to provide treatments with durable, long-term clinical benefit that will halt vision loss in patients. We currently have three ongoing Phase 1/2 clinical programs in IRDs, with an additional program expected to initiate a Phase 1/2 clinical trial in 2019. The targets of our three ongoing Phase 1/2 ophthalmology programs include achromatopsia, or ACHM, related to mutations in *CNGB3*, X-linked retinitis pigmentosa related to mutations in *RPGR*, or XLRP-RPGR, and inherited retinal dystrophy caused by mutations in *RPE65*, or *RPE65*-deficiency. We also have a product candidate that was manufactured and released for compassionate use under a special license in the United Kingdom to treat patients with Leber congenital amaurosis 4, or LCA4, caused by mutations in *AiPL1*. For each of our Phase 1/2 clinical programs we have a prospectively designed natural history study ongoing, which includes the same endpoints as our corresponding gene therapy treatment trial. We believe use of these natural history studies differentiates our programs by providing patient populations to facilitate the efficient execution of our clinical trials and offering insight into the appropriate endpoints for regulatory approval of our gene therapy product candidates. In addition to these clinical programs in IRDs, we have preclinical programs that apply novel approaches to both wet and dry AMD.

The FDA and EMA have granted orphan drug designation to each product candidate in our ongoing clinical programs, including those treating mutations in *CNGB3*, *RPGR* and *RPE65*, as well our product candidate to treat mutations in *AiPL1*. The FDA has also granted rare pediatric disease designation for our clinical programs treating mutations in *RPE65* and *CNGB3* and Fast Track designation to our clinical program treating XLRP caused by mutations in *RPGR*. We have also received PRIME designation from the EMA for our clinical program treating mutations in *CNGB3*.

The deep scientific and clinical understanding of IRDs driving our approach to gene therapy development helps us to optimize our product candidates for each specific genetic mutation and phenotype. We develop our viral vectors by selecting and modifying proprietary cell specific promoters, selecting appropriate capsids for transfection of target cells and refining the vector for efficient production and scalable manufacturing. Not only does this allow us to synergistically target a portfolio of inherited eye conditions, we also believe it has potential to be applied to the development of gene therapies for other diseases.

Our longstanding relationships with leading institutions in retinal disease treatment, including the Moorfields Eye Hospital in London, the University of Michigan Kellogg Eye Center, Massachusetts Eye and Ear, the Medical College of Wisconsin & Froedtert Hospital and the Casey Eye Institute at the Oregon Health & Science University, provide us with access to experts whose guidance and insight informs our development strategy, as well potential patients for our clinical trials.

### ***Our Salivary Gland Programs***

Our second area of clinical focus is xerostomia, a chronic and debilitating disorder of the salivary glands in which saliva production is impaired. Xerostomia may be caused by a number of different insults to the salivary glands, including radiation therapy for head and neck cancer and certain autoimmune diseases. A Phase 1 clinical trial of our gene therapy product candidate, AAV-AQP1, is ongoing in patients who have survived cancer free for five or more years following treatment for head and neck cancer and are suffering from grade 2 or 3 radiation induced late xerostomia, or RIX. There are approximately 170,000 grade 2 or 3 RIX patients who have survived two or more years after radiation treatment for head and neck cancer in the United States, with approximately 10,000 new cases each year. We also intend to initiate a Phase 1/2 clinical trial of AAV-AQP1 for the treatment of patients with chronic xerostomia caused by Sjogren's syndrome, an autoimmune disease affecting more than two million people in the United States.

The FDA has granted orphan drug designation to AAV-AQP1.

### ***Our Neurodegenerative Disease Programs***

Neurodegenerative diseases are our third area of focus. Our first target indication is ALS and we expect to file an investigational new drug application, or IND, for our first neurodegenerative disease product candidate in 2019. We believe our approach to treating ALS patients is differentiated because, rather than targeting a specific genetic defect that defines a small subset of ALS patients, we aim to target the underlying cell biology driving motor neuron death in ALS, potentially enabling us to treat a broader patient population that includes both sporadic and inherited forms of the disease. Increasing evidence suggests a critical role of RNA metabolism in neuronal cells, in particular in motor neurons that are specifically affected in ALS. We believe that dysregulation of neuronal RNA processes results in the degeneration of motor neurons that leads to ALS. Using our viral vector product candidate, AAV-UPF1, we target the central quality control system regulating RNA in motor neurons with the aim of enhancing motor neuron survival in ALS patients.

We have an Alzheimer's disease program that is likewise directed towards the underlying cell biology of the disease, in this case endosomal trafficking, a mechanism cells use to cycle proteins to the cell surface. Over the past decade, evidence has emerged supporting endosomal trafficking dysfunction in neurons as a central process in the early etiology of Alzheimer's disease. In particular, a master regulator of trafficking out of the endosomes called retromer has been implicated. We are in the process of identifying what we believe to be the optimal approach to restoring normal endosomal function to the neurons that are the first to be affected in Alzheimer's. In parallel, we are developing and validating biomarkers of endosomal dysfunction and pre-symptomatic Alzheimer's disease. We believe this approach may also provide a framework for treating certain forms of Parkinson's disease that are also associated with endosomal dysfunction.

### ***Our Strengths***

In addition to our four ongoing clinical programs, we have a broad pipeline of preclinical programs, core capabilities in viral vector design and optimization, gene therapy manufacturing and a potentially transformative gene regulation technology. Utilizing the following key strengths, we aim to develop, commercialize and expand our portfolio of product candidates.

- **Deep Expertise in Gene Therapy Development:** We believe our expertise in viral vector design, optimization and process development allows us to efficiently advance gene therapy products candidates from preclinical development to cGMP manufacturing and clinical development through commercialization.
- **Potentially Transformative Gene Regulation Technology Platform:** We are developing proprietary technology to enable innovative gene therapy treatments whose expression can be

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turned on and off with an easily administered small molecule. We believe the capacity for temporal control of gene therapy products has the potential to transform the gene therapy landscape by opening up new treatment possibilities.

- **Manufacturing Capabilities and Capacity:** We have a flexible and scalable cGMP manufacturing facility and production process, which we expect can supply all of our current clinical and preclinical programs through regulatory approval and, should they be approved, provide sufficient capacity for their commercial production.
- **Robust and Diverse Clinical and Preclinical Pipeline:** Applying our portfolio approach to gene therapy product development, our initial focus is on treatments for IRDs, salivary glands disorders and neurodegenerative diseases with potential for accelerated approval and has produced four ongoing clinical programs and multiple preclinical development programs.
- **Relationships with Leading Institutions:** Our longstanding relationships with leading institutions and experts provides us with guidance on development strategy and access to potential patients for our clinical trials.
- **Natural History Study Data:** We sponsor ongoing prospective long-term natural history studies in IRDs that facilitate our ability to efficiently enroll our treatment studies, potentially reducing clinical trial timelines and providing insight into the appropriate endpoints for regulatory approval.

### **Our Strategy**

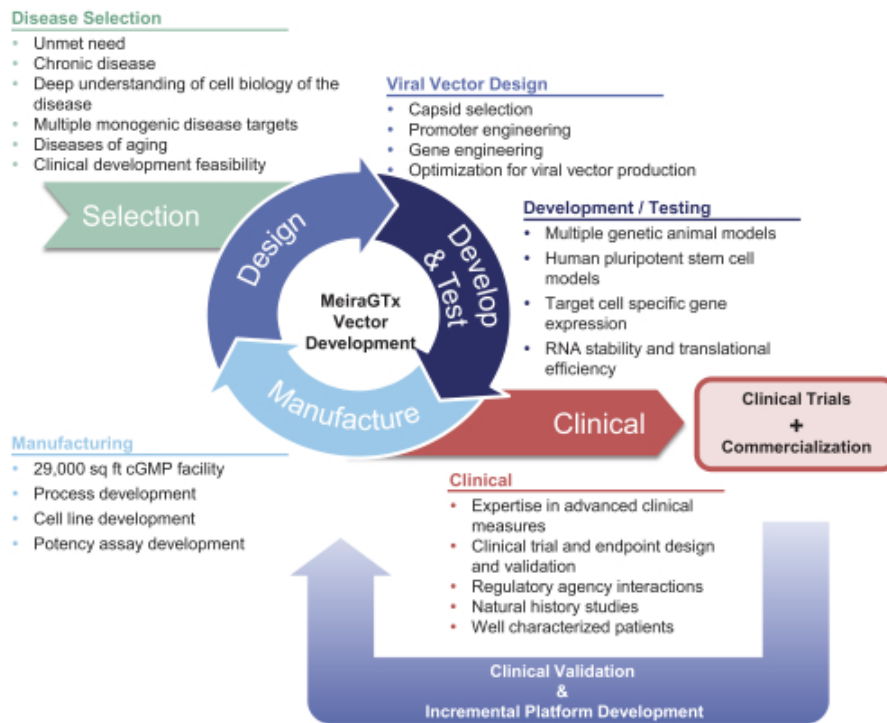
Our goal is to develop and commercialize innovative gene therapy products to treat serious disorders and broaden the scope of indications that may be treatable by our gene therapies. Our strategy to achieve this goal is to:

- successfully complete clinical development, obtain regulatory approval and commercialize our pipeline of gene therapy product candidates to treat disorders of the eye and salivary gland;
- continue to advance the development of our pipeline of product candidates for the treatment of neurodegenerative disorders;
- utilize our viral vector design and optimization capabilities to identify and develop new gene therapies for other serious diseases;
- advance the development of our potentially transformative proprietary technology for regulating the activity of gene therapy products using small molecules and initiate clinical trials of new product candidates; and
- evaluate strategic collaborations with other biotechnology and pharmaceutical companies to leverage our capabilities, manufacturing capacity and proprietary gene regulation technology.



The figure below depicts the steps in our product engine, including disease selection, design, development/testing, clinical and manufacturing:

## MeiraGTx Product Engine



### Gene Therapy Overview

Gene therapy uses a delivery vehicle, referred to as a vector, to insert a functionally active gene into cells in the body. The gene encodes a therapeutic protein that may block disease pathways or may enhance a deficient pathway. Gene therapy has been studied for over 50 years, with a variety of different viral vectors employed to deliver therapeutic genes. Since the first clinical study of therapeutic gene transfer in humans in 1990, more than 2,300 gene therapy studies covering a broad range of disease targets have been initiated. Recently, the first gene therapies have received regulatory approval, including approval by the FDA of Luxturna for an ophthalmology condition, resulting in a growing acceptance of gene therapy technology as a potentially safe and effective therapeutic approach.

Our current programs use the adeno-associated virus, or AAV, as the vector for delivering gene sequences into a patient’s cells. The key components of an AAV vector include: (i) the capsid, or the outer viral protein shell that encloses the target DNA, which is responsible for binding to the cell surface and allowing the therapeutic gene that it is carrying to enter the cell; (ii) the therapeutic gene, or transgene, that encodes the therapeutic protein; and (iii) the promoter, or the DNA sequence that drives the expression of the transgene. AAV is a good vector for gene therapy delivery because of its relative safety and broad applicability. AAV is less immunogenic, or less prone to causing an immune reaction, than previous generations of gene therapy vectors, such as adenoviral vectors and AAV does not readily integrate into the genome of the target cell, reducing the potential for oncogenesis, or the induction of cancer. AAV vectors can transfer a therapeutic gene into, or transduce, numerous cell types. Slight differences in capsid proteins can modulate the efficiency with which

different capsids deliver genes to different cells, thus allowing different AAV capsids to be selected to most effectively target particular cell types.

The therapeutic gene sequence that enters the targeted cell includes both the protein coding region and an engineered promoter sequence that is used to drive functional gene expression. These engineered promoters may be designed to drive different levels of gene expression or to limit gene expression to specific cell types. Additional aspects of the transgene sequence may be engineered for optimal gene expression, such as codon usage and synthetic introns, which may enhance levels of therapeutic protein expression.

Gene therapy can be used to address monogenic diseases, which result mutations in a single gene in a patient's genome. In such cases, the viral vector is used to deliver a normal copy of the gene to the cells that are defective due to the lack of the gene function. The normal gene then drives production of the missing protein and offers a therapeutic benefit in patients with the disease. This gene replacement approach underlies all of our clinical IRD programs.

Rather than replacing a gene that is defective or missing in a monogenic disease, gene therapy can also provide a therapeutic impact by adding a particular new gene function to cells and thereby change cell behavior and function. This is the aim of our salivary gland programs, where our treatment is designed to promote water to flow through otherwise impermeable cells in damaged salivary glands and increase saliva flow into the mouth. Additionally, gene therapy may be used to deliver a therapeutic protein that may block a disease pathway or enhance a deficient cellular pathway in multifactorial diseases such as wet AMD and neurodegenerative diseases, including ALS and Alzheimer's disease.

Importantly, AAV vectors enable targeting of therapeutic genes to non-dividing cells, in which they are thought to remain for the rest of the cell's life. This means that a single treatment may offer patients a durable effect and long term benefit. The specific cells of the eye, salivary gland and the neurons that we target in our current gene therapy programs are largely non-dividing cells and preclinical evidence has shown that they can be effectively targeted by the specific AAV capsids that we use, enabling us to potentially achieve a durable impact on each of the diseases that we treat.

## **Our Ophthalmology Programs**

### ***Overview and Strategy***

We currently have three ongoing Phase 1/2 clinical programs targeting IRDs, including ACHM related to mutations in *CNGB3*, *XLRP-RPGR* and *RPE65*-deficiency, with an additional program expected to enter a Phase 1/2 clinical trial in 2019 in patients with ACHM related to mutations in *CNGA3*. We also have a product candidate that was manufactured and released for compassionate use under a special license in the UK to treat LCA4 patients. We chose diseases of the eye as our first area of clinical focus because we believe the eye is ideally suited for gene therapy for the following reasons.

- The eye is easily accessible and has highly compartmentalized anatomy, which allows for accurate delivery of vectors to specific tissues using direct visualization and microsurgical techniques.
- The structure of the eye allows for efficient delivery to specific cell subtypes with small volumes of vector, making the dose per patient much lower than for systemic treatment.
- Anatomical barriers and unique structure of the eye make the immune response to the intraocular administration of vectors more attenuated than systemic administration.
- Largely non-dividing cell populations in the eye make good targets for potentially stable, long-term gene delivery and expression.

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- The retina, a structure in the back of the eye, is visible and there are many well validated structural and functional readouts allowing the detailed assessment of the therapeutic impact of the gene therapy treatment.

Our strategy for developing gene therapies targeting eye diseases is to begin with a number of monogenic IRDs that are good candidates for gene replacement therapies and expand to more common eye diseases over time. We have taken a portfolio approach to the development of IRDs because, while some of these genetic defects are rare, IRDs as a class are one of the most common causes of blindness in working age adults and there are multiple synergies at the clinical, regulatory and commercial levels between many of these diseases caused by different gene mutations.

Two of our clinical-stage product candidates are targeting IRD indications in achromatopsia caused by mutations in the *CNGB3* gene and inherited retinal dystrophy caused by mutations in the *RPE65* gene. The primary defect in these particular genetic disorders is the absence of function of one of the two different types of photoreceptors that constitute the light sensing part of the retina, rods or cones. In achromatopsia, the cones completely lack function, while in *RPE65*-deficiency it is the rods that lack function. In these indications, we anticipate that restoring a normal copy of the mutant gene to the retina of patients with these genetic disorders may restore function to the particular type of photoreceptor that is defective in each of these indications. Although cone photoreceptors are generally preserved during childhood in *RPE65*-deficient patients, the lack of healthy active rods eventually affects the cones that they support and over time both rods and cones die, the retina degenerates and *RPE65*-deficient patients become totally blind.

We also have a clinical-stage product candidate for XLRP-RPGR, in which all photoreceptors, both rods and cones, function poorly, leading to degeneration of the retina and total blindness. We have used data and learnings from our *RPE65* studies to inform the design and techniques used in our XLRP-RPGR program. The aim of our XLRP-RPGR treatment is to slow the degeneration of the retina, which we measure using validated surrogate structural endpoints and changes in the detailed structural maps of these patients' retinas over time.

In order to expand our gene therapy pipeline for retinal diseases, we are also developing treatments for certain multifactorial eye diseases, which are diseases caused by multiple genetic or environmental factors. We have a preclinical program using an anti-VEGFR2 antibody targeting wet AMD and we anticipate filing an IND for this program by the end of 2019. We are also working to integrate our gene regulation technology with our wet AMD program. Our ultimate aim is to activate the anti-VEGFR2 antibody gene that we have installed in the eye with a small molecule applied topically in an eye drop. This could potentially allow for intermittent dosing of the antibody using an eye drop rather than injection. Additionally, we are developing a novel approach to treat advanced dry AMD patients who have lost central vision through our innovative "rod-to-cone" technology. By genetically engineering rods with molecules that will improve their speed of response to light, we aim to effectively transform a patch of rod photoreceptors in the outer part of the retina to behave more like cone photoreceptors, thus improving vision.

We intend to leverage our platform to take advantage of the many synergies across our ophthalmology programs, including identification, diagnosis and characterization of patients, specialized surgical techniques, clinical and regulatory process, vector production and cGMP manufacturing, as well as commercial synergies, if these product candidates are approved by the FDA and other regulatory authorities.

### ***Our Competitive Advantage: Natural History Studies, Relationships with Leading Institutions and Our cGMP Manufacturing Facility***

IRDs as a class are the most common cause of blindness in the working age population worldwide and a leading cause of impaired vision in children in developed countries. There are approximately 200,000 people in each of the United States and European Union affected by IRDs. However, IRDs may be caused by mutations in over 200 identified genes, and in many cases each genetically defined IRD may be a small patient population. Meaningful clinical trials for these sorts of rare indications are especially challenging because they require access

to sufficient patients and baseline data on each patient in order to secure clear indicators of efficacy as a result of intervention. We seek to address this problem by sponsoring prospectively designed natural history studies in each of the indications that we are treating in our Phase 1/2 trials.

The lead investigator for the natural history studies is Michel Michaelides, Professor of Ophthalmology at Moorfields Eye Hospital in London. For each of the natural history studies, baseline assessments are made upon enrollment, with follow up assessments at six month intervals for two years and annual assessments for up to an additional three years. A broad range of assessments are used, including functional tests, retinal imaging and electrophysiological assessments. The same assessments used for each natural history study are used in our corresponding clinical trial targeting the same indication, allowing us to compare the impact of our product candidates on the progression of these diseases on a population, as well as individual patient basis.

We expect the natural history studies will enhance our understanding of disease progression for each indication we are targeting and allow us to identify optimal windows for intervention, provide specific functional and structural parameters to quantify treatment effects and define clinical endpoints. These studies also provide us with a source of potential patients for our treatment studies and have facilitated efficient enrollment of these studies. These patients are not only genotyped, but have up to five years of detailed functional and structural assessment data prior to enrollment into an appropriate treatment study.

We also have longstanding active relationships and clinical site agreements with leading institutions in retinal disorder treatments, including Moorfields Eye Hospital in London, the University of Michigan Kellogg Eye Center, Massachusetts Eye and Ear, the Medical College of Wisconsin & Froedtert Hospital and the Casey Eye Institute at the Oregon Health & Science University. Our relationships with these institutions, in most cases, precede the date on which we entered into a clinical site agreement with the applicable institution. Professor Robin Ali, Ph.D., our Head of Preclinical Ophthalmology and one of our founders, is Professor of Human Molecular Genetics at UCL Institute of Ophthalmology and Theme Leader for Gene Therapy at NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital in London, and a Visiting Professor at the University of Michigan Kellogg Eye Center. These institutions are among the premier treatment centers for the indications that we are pursuing and provide us with access to potential patients for our clinical trials and experts in IRDs who offer strategic guidance and expertise for our development strategy. These institutions provide services with respect to our preclinical and clinical studies. For example, our AAV-CNBG3 clinical trial is being conducted at Moorfields Eye Hospital in London, and surgeries for our AAV-RPE65 clinical trial have been performed there and at University of Michigan Kellogg Eye Center. Participants enrolled at the University of Michigan Kellogg Eye Center for our RPE65-deficiency natural history study travel to the Medical College of Wisconsin & Froedtert Hospital for adaptive optic assessments. The Casey Eye Institute at the Oregon Health & Science University provides certain reading center and other clinical services with respect to our clinical trials. University of Michigan Kellogg Eye Center, Medical College of Wisconsin & Froedtert Hospital and Massachusetts Eye and Ear each provide services in relation to our natural history study for *XLRP-RPGR*.

We believe our flexible and scalable cGMP compliant manufacturing facility has sufficient capacity to support the development needs for our current clinical and preclinical ophthalmology programs, and commercial needs, if our product candidates are approved by the FDA and other regulatory authorities.

### ***Achromatopsia***

#### *Disease Background and Market Opportunity*

Achromatopsia, or ACHM, is an IRD that specifically prevents cone photoreceptors from functioning. ACHM patients are legally blind from birth and usually suffer from severely reduced visual acuity of 20/200 or worse, a disabling sensitivity to light, or photoaversion, total color blindness and involuntary back and forth eye movements, or nystagmus.

Cones and rods are the two kinds of photoreceptors in the human eye. Photoreceptors are light-sensitive cells that absorb light and convert it into an electrical signal that is transmitted to the brain for the perception of

light, or vision. Rods can detect very low levels of light and are quickly inactivated in higher light levels, enabling vision in dim light. Cones, on the other hand, remain active in high light levels and support daytime vision and the perception of color. Even though only 5% of the photoreceptors in the eye are cones, they are concentrated in the central part of the retina, the macula, where they are tightly packed, thus enabling high-acuity daytime vision. The highest cone density is in the centermost spot of the macula, called the fovea. Since cones are essential for central visual acuity, color vision, and most daily visual activities, ACHM patients suffer significant vision loss due to the complete lack of cone function.

ACHM occurs in approximately one in 30,000 people in the United States. To date, mutations of any one of six genes encoding components of the light sensing machinery of cone photoreceptors have been identified as causing ACHM. The *CNGB3* and *CNGA3* genes are the two most common of these genes, together accounting for up to 92% of ACHM cases, with *CNGB3* slightly more common than *CNGA3* in most geographic territories. Together, the proteins encoded by the *CNGB3* and *CNGA3* genes make up the cone-specific cyclic nucleotide gated, or CNG, channel, which is essential for cones to produce an electrical signal in response to light. Mutations in either of these genes prevent the formation of the CNG channel.

There are estimated to be approximately 12,000 patients with ACHM caused by mutations in *CNGB3* in the United States, Japan and Germany, France, Spain, Italy and the United Kingdom, or the EU5, with about 25% of those patients being under the age of 18 and approximately 125 new cases being diagnosed annually. We believe the availability of a therapeutic option may increase patient identification and the estimated prevalence of ACHM.

### *Our Gene Therapy Program*

We have designed specifically optimized gene therapy viral vector candidates to treat ACHM caused by mutations in each of *CNGB3* and *CNGA3*, with which we aim to address the majority of patients suffering from ACHM. Our product candidates are delivered via subretinal injection covering the central macula region of the eye, where most of the cones in the retina are located.

ACHM is predominantly a stationary disease, which means that ACHM patients' retinas contain non-functioning cones that survive intact for many decades. This is in contrast to many IRDs in which the entire retina slowly degenerates over a patient's life. This extended survival of cones with their potential for light sensitivity presents a wide window of opportunity to introduce a normal copy of the mutated gene via a gene therapy product candidate and thereby restore cone function. While the stationary nature of ACHM means that cones remain present for decades, the functional connections between active cones and the visual cortex in the brain are thought to become fixed in teenage years. Therefore, we believe that younger individuals are likely to benefit most from gene therapy treatment for ACHM because of their greater visual plasticity. Another debilitating symptom of ACHM, which lasts throughout life, is photoaversion. A disabling and ubiquitous symptom of ACHM, photoaversion is the avoidance of light due to discomfort in the presence of levels of light equivalent to a normally lit room or daylight. ACHM patients often avoid light and wear dark glasses, which further diminishes their already very poor vision. We believe it is possible that restoration of cone function in adult patients might have an impact on photoaversion even if brain plasticity is limited.

We believe that gene therapy treatment for ACHM in which we aim to restore cone function via a gene replacement strategy may offer benefits across a range of ages, which we aim to define in our clinical development programs.

### *ACHM Caused By Mutations in CNGB3*

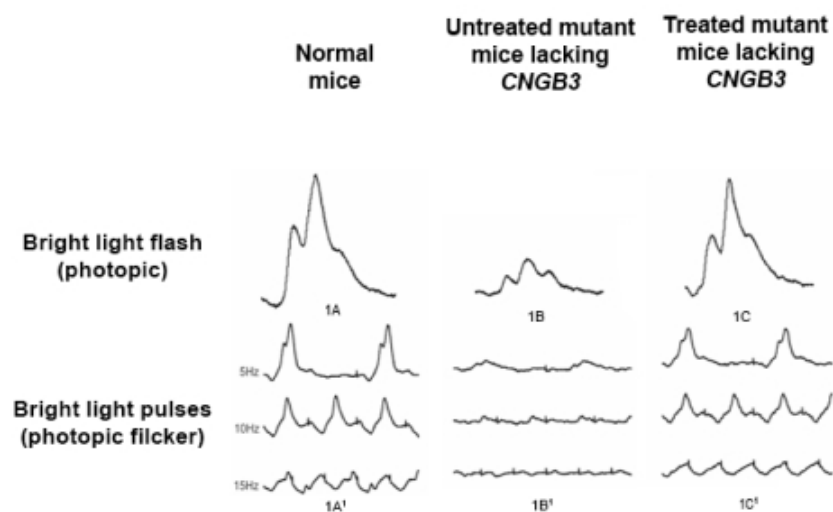
With our collaborators at the University College of London's Institute of Ophthalmology, or UCL IO, led by Professor Robin Ali, we have developed a product candidate to treat ACHM caused by mutations in the *CNGB3* gene. Mutations in the *CNGB3* gene prevent cone photoreceptors from functioning because *CNGB3*'s gene product is integral to the formation of a specific membrane channel that enables cones' electrical response to light. *CNGB3* is a gene exclusively expressed in cones and our aim is to replace the absent function of the mutant *CNGB3* gene with a normal copy of the gene in cones of IRD patients and thereby restore cone function.

In order to drive expression of the functional gene specifically in cones and not in other cells of the retina, we use the cone specific human cone arrestin, or CAR, promoter to drive the expression of a codon optimized *CNGB3* cDNA. Codon optimization improves protein expression by increasing translation efficiency. To transfect cone photoreceptors, we use the AAV8 capsid, which enables the efficient delivery of the *CNGB3* gene cargo to those photoreceptors. As the vast majority of the cones in the eye are located centrally and concentrated in the macula, we treat this central region of the retina through subretinal injection to deliver the viral vector product candidate to the photoreceptors in which its activity is required.

Preclinical studies in mice lacking the *Cnrgb3* gene were carried out by our collaborators at UCL IO and led by Professor Robin Ali in 2010 and 2011 and the data was published in *Human Molecular Genetics* in 2011. In these studies, it was observed that delivery of our *CNGB3* product candidate, AAV-CNGB3, via subretinal injection at doses between  $6E^9$  and  $8E^9$  viral genomes per eye, or vg/eye, was associated with a restoration of cone function to near normal levels.

In one of these studies, retinal response to light was measured in three groups of mice: *Cnrgb3* mutant mice treated with AAV-CNGB3, untreated *Cnrgb3* mutant mice and normal mice. Mice were treated with AAV-CNGB3 vector dosed at  $2E^{12}$  vg/mL ( $8E^9$  vg/eye) via subretinal injection. One eye was treated per mouse. Vector was administered when mice were 30 days old, and electrical responses, or ERGs, of the retina were measured 90 days following administration of the vector.

Figure 1 shows representative ERG responses of the retina to different light stimuli: a single flash of bright light (1A; 1B; 1C) and repeated pulses, or flickers, of bright light at different frequencies to assess the refresh rate of the photoreceptors (1A'; 1B'; 1C'). Retinas from three different groups of mice were tested: retinas of normal mice (Figure 1A), retinas of mutant mice lacking the *Cnrgb3* gene (Figure 1B) and retinas of mutant mice lacking the *Cnrgb3* gene, but treated with AAV-CNGB3 (Figure 1C). It was observed that the response to a bright light pulse was largely absent in the retinas of *Cnrgb3* mutant mice, as this response is largely mediated by the cones and is therefore severely impacted by the *Cnrgb3* mutation (Figure 1B). It was also observed that treatment of *Cnrgb3* mutant mice with AAV-CNGB3 was associated with a high-degree of restored cone function in these mutant mouse retinas in response to a single flash of bright light (Figure 1C). In addition, we tested the response of cones to rapid flickers of bright light (Figure 1A') because only cones can register multiple sequential signals from rapid flickers. It was observed that registering rapid flickers was also impacted by the *Cnrgb3* mutation (Figure 1B') and the cone flicker response was nearly completely restored in the retinas of *Cnrgb3* mutant mice following treatment with AAV-CNGB3 (Figure 1C').



**Figure 1.** Electrical responses of the retina reacting to two different light stimuli: a single flash of bright light and repeat pulses of bright light at increasing frequency, or flickers.

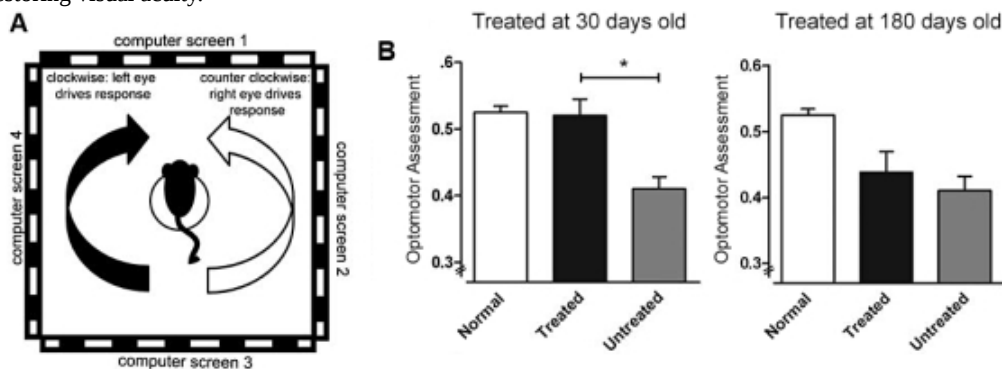
**Figure 1A and 1A'.** The electrical responses of the retina from a normal mouse reacting to a flash of bright light and flickers.

**Figure 1B and 1B'.** The electrical responses of the retina from a mutant mouse lacking *Cngb3* reacting to a flash of bright light and flickers.

**Figure 1C and 1C'.** The electrical responses of the retina from a mutant mouse lacking *Cngb3* treated with AAV-CNGB3 reacting to a flash of bright light and flickers. Treatment with AAV-CNGB3 was associated with a high degree of restoration of cone function, with the electrical response to a bright flash of light and rapid flickers nearly matching the response observed in the normal mouse retina.

In another one of the preclinical studies carried out by our collaborators at UCL IO, it was assessed whether functional improvement at the retinal level of *Cngb3* mutant mice was impacted by the age of the mice at the time treatment with the gene therapy product candidate. In this study, *Cngb3*-mutant mice were treated with AAV-CNGB3 at 30 days old, the P30 group, or 180 days old, the P180 group. One eye was treated in each mouse via subretinal injection dosed at  $2E^{12}$  vg/mL ( $8E^9$  vg/eye). Optomotor measurements were taken 60 days after treatment of the P30 group of the *Cngb3* mutant mice treated with AAV-CNGB3 (n=11), untreated *Cngb3* mutant mice (n=11) and normal, age-matched untreated mice (n=5). Optomotor measurements were also taken 60 days after the treatment of the P180 group of the *Cngb3* mutant mice treated with AAV-CNGB3 (n=6), untreated *Cngb3* mutant mice (n=6) and normal, age-matched untreated mice (n=5). Optomotor assessments were made by placing each mouse on a pedestal located in the center of four inward facing computer screens, that projected a rotating image. The head-tracking responses of each mouse was observed using an overhead infrared video camera. Visual acuity was measured by involuntary reflex head-tracking responses driven by the left (clockwise rotations, black arrow) and right (counter-clockwise rotations, white arrow) eyes, respectively (Figure 2A).

Figure 2B is a graph comparing the visual acuity as measured by the average optomotor assessment of the normal eyes, eyes from *Cngb3* mutant mice treated with AAV-CNGB3 and eyes from *Cngb3*-mutant mice that were untreated. It was observed that *Cngb3* mutant mice had a significantly lower visual acuity than normal mice. However, after treatment with AAV-CNGB3, visual acuity in the *Cngb3* mutant mice eyes treated at 30 days old was observed to be restored to a similar level as that observed in normal mice. In contrast, no significant difference in visual acuity between the treated and untreated eyes was observed when treatment was given at 180 days old. Data from this study suggests that treatment received at an older age is less capable of restoring visual acuity.



**Figure 2A.** Depiction of how optomotor assessments were taken. Each mouse was placed on a pedestal located in the center of four inward facing screens and was observed by an overhead infrared video camera. The assessments were made 60 days following treatment of the *Cngb3* mutant mice with AAV-CNGB3 at 30 days old and 180 days old.

**Figure 2B.** Graph showing averaged optomotor assessment of each group. Visual acuity, as measured by the optomotor assessment, was observed to be restored to normal levels in the mouse treated at 30 days old (left panel) but not in the mouse treated at 180 days old (right panel).

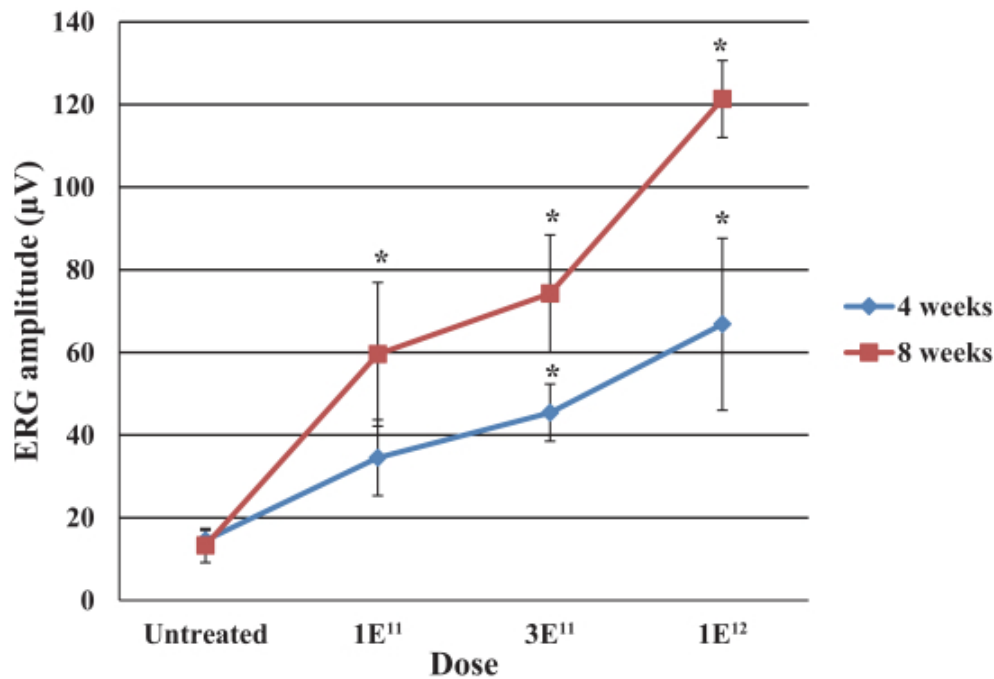
Between October 2016 and December 2016, we carried out a dose-ranging preclinical study at UCL IO to determine the efficacy of different doses of AAV-CNGB3 in rescuing cone response to a single pulse of bright light in *Cngb3* mutant mice as measured by electrical responses across the retina, or ERG. The study was conducted to support a planned Phase 1/2 clinical trial in patients with *CNGB3* mutations following the FDA's request for additional rescue data at a range of different doses. While long-term functional rescue was observed in prior tests, there was no dosage titration tested in those studies. The data from this study has not been published.

We assessed cone-mediated ERG responses in *Cngb3* mutant mice at three doses and compared these responses to baseline recordings of untreated eyes at two different time-points following treatment. *Cngb3* mutant mice were administered AAV-CNGB3 via subretinal injection of 4 $\mu$ L of vector at each dose. Mice were treated at four weeks of age and ERG responses were measured in these mice at four weeks and eight weeks following treatment. Three eyes were treated at each of the three doses, and three eyes were untreated. The reviewer analyzing the ERG traces was masked to which eye received treatment.

Figure 3 shows the photopic ERG amplitudes measured to assess cone photoreceptor function in *Cngb3* mutant mice treated with AAV-CNGB3 at 1E<sup>11</sup> vg/mL (4E<sup>8</sup> vg/eye; n=3), 3E<sup>11</sup> vg/mL (1.2E<sup>9</sup> vg/eye; n=3) and 1E<sup>12</sup> vg/mL (4E<sup>9</sup> vg/eye; n=3), and untreated eyes (n=3) at four and eight weeks post administration. A photopic ERG is the electrical response of the retina corresponding to cone electrical activity following a single pulse of bright light (single ERG recordings are shown in Figure 1). The higher the ERG amplitude, the greater the response of the retina to bright light. These data show a statistically significant increase in cone ERG responses for all three doses of AAV-CNGB3 and for both time-points following vector administration except for low dose at four weeks post injection (p=0.051). These data indicate that AAV-CNGB3 is associated with the rescue of the cone electrical response in the retina of *Cngb3* mutant mice in a dose-responsive fashion. While initial responses were observed in mice four weeks after subretinal injection of the vector, at all three doses significantly stronger ERG responses were observed eight weeks after vector administration, with the maximum ERG response observed at the highest dose eight weeks after administration.

In this study, a dose response in ERG amplitudes from treated eyes was observed, suggesting that increasing amounts of AAV-CNGB3 is associated with greater rescue of responses in *Cngb3* mutant mice. The three doses tested in this study are the same as those doses administered in our AAV-CNGB3 Phase 1/2 clinical trial on a vg/mL of viral vector titer basis.





**Figure 3.** Graph of averaged photopic ERG amplitudes at four and eight week time-points post administration of AAV-CNGB in *Cngb3* mutant mice treated at four weeks of age. The blue line indicates the electrical response amplitudes observed following administration of different doses of AAV-CNGB3 measured at four weeks after treatment. The red line shows the increased level of electrical response observed in the same mice treated with AAV-CNGB3 four weeks later, at eight weeks following treatment. This is compared to the ERG response in untreated eyes, which remained unchanged at both time points.

During 2016, we conducted three preclinical toxicology studies of AAV-CNGB3 at UCL IO. We conducted a nine month study in normal mice in which four eyes were dosed with saline as a control, nine eyes were dosed at 2E<sup>9</sup> vg/eye, and nine eyes were dosed at 4E<sup>9</sup> vg/eye, with a toxicology assessment at one, three, six and nine months post-administration. We also conducted an eight week study in normal mice, in which 15 mice were dosed with saline as a control, 15 mice were dosed at 2E<sup>9</sup> vg/eye, and 15 mice were dosed at 4E<sup>9</sup> vg/eye, providing five mice from each group for studying local and systemic effects at each time-point of one, four and eight weeks after treatment. We also conducted an eight week rabbit study in which the right eyes of nine animals were dosed with saline as a control, the right eyes of nine animals were dosed at 0.8E<sup>11</sup> vg/eye and the right eyes of nine animals were dosed at 2.4E<sup>11</sup> vg/eye, providing three animals from each dose group for studying local and systemic effects at each time-point of one, four and eight weeks after treatment. Biodistribution was examined in the eight week mouse and rabbit studies. No harmful effects on the retina or systemically were observed at the time-points listed after treatment. The data from these studies have not been published. We used these data to support our clinical trial application, or CTA, and IND for treatment of patients with ACHM related to *CNGB3* mutations with AAV-CNGB3.

### *Clinical Development of AAV-CNGB3*

We have an ongoing natural history study in ACHM including over 90 patients that allows us to collect structural and functional data for up to five years on prospectively defined endpoints, including functional tests (visual acuity, contrast sensitivity, mobility maze and photoaversion assessments), retinal imaging (color fundus photography, fundus autofluorescence imaging, spectral domain optical coherence tomography and visual field testing) and electrophysiological assessments. The study center is the Moorfields Eye Hospital in London. We believe access to these ACHM patients has enabled us to efficiently enroll the most appropriate patients into our *CNGB3* Phase 1/2 clinical trial. We intend to present this natural history data to regulatory agencies for discussion of our pivotal trial design and path to regulatory approval. In addition to giving us access to patients and potentially accelerated enrollment in our treatment studies, we believe the prospective natural history data on each treated patient allow us to gather robust data from our Phase 1/2 clinical trial in a condensed timeframe.

We are conducting a Phase 1/2 clinical trial of AAV-CNGB3 in both adult and pediatric patients. In the dose escalation phase of the trial, up to 18 adult patients (18 years or older) may be administered one of three different doses of vector in dose escalating cohorts of three to six patients at a time. Once an acceptable safety profile has been established in adults, up to nine children may be treated at an acceptable dose. We will close out this trial six months after the last pediatric patient has been treated. Six months following treatment, each patient moves onto a long term follow up study in which they are followed for safety and indication of benefit for an additional four and a half years.

The primary endpoint of this open-label, dose-escalation clinical trial is the safety of a one-time subretinal administration of AAV-CNGB3 in patients with ACHM caused by *CNGB3* mutations. Secondary endpoints include the outcomes of a range of functional assessments and detailed structural analysis of the retina, including imaging of individual photoreceptors.

This trial is open in the United Kingdom under our CTA. We have treated 10 adult patients at the Moorfields Eye Hospital in London, including three patients at the highest proposed dose.

We submitted our IND for AAV-CNGB3 to the FDA in the fourth quarter of 2017. The IND has not yet been opened because we received a question from the FDA regarding our injection device compatibility assay, thus putting the IND on clinical hold until we have satisfactorily answered the FDA's question and the clinical hold is lifted by the FDA. In the device compatibility assay the FDA noted a disparity between the target titer for the intended low dose dilution and the actual titer obtained on polymerase chain reaction, or PCR, analysis. The FDA requested clarification on whether this was an imprecise dilution scheme for the low dose or a PCR assay issue. We submitted a response to the FDA on May 2, 2018 providing data that identified the issue as a PCR assay artifact and also showing data that we believe supports that this has now been addressed. Although we are unable to extend the ongoing study to sites in the United States until the clinical hold is lifted, we continue to treat patients in the UK under our CTA.

In this trial, AAV-CNGB3 viral vector is delivered via subretinal injection of up to 0.5mL targeting the central region of the retina, including the macula and fovea, where most of the cones are located. One eye is treated in each patient, which is the eye assessed to be the worst eye at baseline. We have treated 10 adult patients (between 18 and 33 years old) in the dose escalation phase of our Phase 1/2 clinical trial. These 10 patients were dosed in three cohorts with escalating doses of  $1E^{11}$  vg/mL (cohort one),  $3E^{11}$  vg/mL (cohort two) and  $1E^{12}$  vg/mL (cohort three) of AAV-CNGB3.

In each of the 10 patients treated, the macula, including the fovea, was covered by the subretinal injection. Subretinal injections have been administered by two different surgeons at the Moorfields Eye Hospital in London.

In adult *CNGB3* patients, treatment of the central retina with our AAV-CNGB3 product candidate via subretinal injection has been generally well tolerated. Following the review of the safety data for each cohort

treated in this study, the independent monitoring committee, or IDMC, recommended escalation to the higher dose in the next cohort. Data from the first adult treatment cohort along with our preclinical data of AAV-CNGB3 was used to support our PRIME designation that was awarded by the EMA in February 2018.

As of May 4, 2018, all three patients in cohort one and the first patient in cohort two have completed the first six months of follow up after treatment and have moved into the long term follow up protocol. In this timeframe we have not yet observed changes in visual function assessment in these adult patients. However, we have observed signs of improvement in measurements of photoaversion in two of the four patients in the treated eye compared to baseline. This preliminary observation has been observed at both the three and six month assessments following treatment in both patients. This is preliminary data and measurements must be repeated at further time points and in additional patients to support any potential effect. In this clinical trial, photoaversion is assessed by measuring changes in the opening between the upper and lower eyelids, or the palpebral aperture, in response to exposure to light of 16.6 cd/cdm<sup>2</sup> in patients following treatment compared to pretreatment baseline. As discussed in *Investigative Ophthalmology & Visual Science* in 2017, this is a surrogate endpoint of photoaversion in ACHM patients.

We anticipate completing dosing in our *CNGB3* Phase 1/2 clinical trial, including the pediatric dosing, in the second half of 2018. We expect to release data from the adult dose escalation cohorts along with preliminary six month data from the pediatric patients in 2019.

With this data, we plan to meet with the regulatory agencies in 2019 to discuss the pivotal trial design and path to regulatory approval, with the aim of initiating a pivotal trial in *CNGB3* patients in 2019.

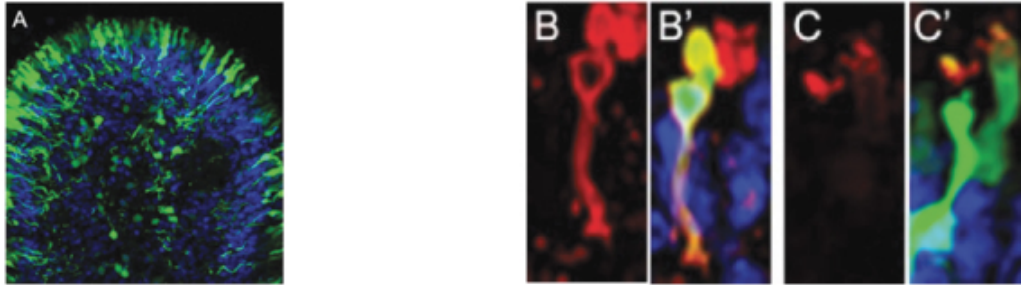
Our *CNGB3* gene therapy product candidate, AAV-CNGB3, was granted orphan drug designation by the FDA and EMA, as well as rare pediatric disease designation by the FDA for the treatment of achromatopsia caused by mutations in the *CNGB3* gene. We have also been granted PRIME designation by the EMA.

#### *ACHM Caused by Mutations in CNGA3*

We are also developing AAV-CNGA3 to treat ACHM caused by mutations in the *CNGA3* gene. While the mechanism for treating *CNGA3* related ACHM is similar to that for *CNGB3*, we believe a larger amount of *CNGA3* protein is required to restore cone function compared to *CNGB3*. We believe this may reflect the 1:3 ratio in which *CNGB3*:*CNGA3* subunits associate to form the cone CNG channel. We have designed a synthetic promoter to drive high levels of *CNGA3* expression specifically in cones. In preclinical studies, our novel cone specific promoter has been associated with strong gene expression in all human cone subtypes in human retinas grown *in vitro* using human pluripotent stem cells, or hPSC. AAV-CNGA3 utilizes this proprietary pan cone promoter to drive a codon optimized *CNGA3* gene sequence. We believe this novel promoter can drive sufficient expression of *CNGA3* in cones to restore light sensitivity to these cones in *CNGA3* deficient patients. We use the AAV8 capsid to transfect cone photoreceptors in the back of the eye and we target the cones concentrated in the central region of the retina via a subretinal injection that covers the macula.

A key aspect of developing an effective treatment for ACHM caused by *CNGA3* mutations is a promoter that drives robust gene expression in all of the three different cone subtypes, S/blue, L/red and M/green. In particular, it is important to evaluate the activity of the promoter in human photoreceptors, which can be achieved prior to treating patients using human stem cell derived retinas. Our relationship with UCL provides access to what we believe is one of the few centers in the world that can generate human “mini retinas,” or HMRs, which are human retinas grown *in vitro* from hPSCs. These HMRs develop from stem cells over several months to form primary photoreceptors arrayed in a spherical structure that resembles many aspects of the human retina and includes all the rod and cone subtypes, allowing us to assess and predict the utility of many aspects of gene therapy vectors for human clinical application.

*In vitro* studies to measure the gene expression driven by our cone specific promoter in human cones using HMRs were conducted at UCL IO during 2017. Figure 4A shows a fully formed HMR that has been transfected with a construct in which our cone specific promoter was associated with the expression of green fluorescent protein, or GFP, a green marker gene. The expression of GFP is seen specifically in cone photoreceptors throughout this HMR, indicating that our promoter is driving robust gene expression in human cones. To support that this promoter drives gene expression in all cone subtypes, GFP expression driven by our promoter was overlaid with markers specific to each of the cone types. Figure 4B is an image of an S/blue cone and Figure 4C is an image of an L/red cone and an M/green cone, with the cone-specific marker labeled in red in each case. The multiple colors in Figures 4B' and 4C' show the overlay of these cone-specific markers with cone specific GFP expression, indicating that our promoter drives gene expression in all cone subtypes in this HMR. The data from these studies have not been published.



**Figure 4A.** An hPSC derived HMR showing GFP expression (green) driven by our promoter in human cones throughout the HMR.

**Figure 4B.** The red marker identifies this cone as an S/blue cone.

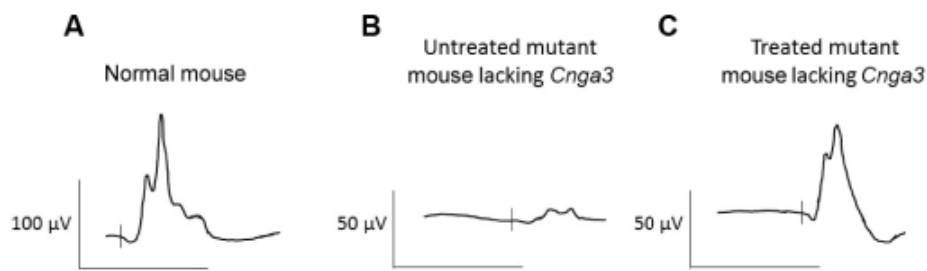
**Figure 4B'.** An overlay of GFP expression from our promoter on top of the S/blue cone specific marker. The overlap between the cone marker and GFP expression indicates that our promoter drives gene expression in S/blue cones.

**Figure 4C.** The red marker identifies M/red and L/green cones.

**Figure 4C'.** An overlay of GFP expression from our promoter on top of the M/Red and L/green cone specific marker. The overlap between the cone marker and GFP expression indicates that our promoter drives gene expression in M/red and L/green cones.

In preclinical studies of mutant mice lacking the *Cnga3* gene conducted at UCL IO during 2017 and 2018, treatment of retinas of *Cnga3* mutant mice with AAV-CNGA3 was associated with restoration of the cone electrical response following subretinal delivery. Figure 5 and Figure 6 show the rescue of cone function that was observed in two of these studies with doses spanning those proposed in the clinical trial and in a dose dependent manner. We believe this supports the evaluation of AAV-CNGA3 to treat patients with ACHM caused by mutations in *CNGA3* in a Phase 1/2 clinical trial. The data from these studies have not been published.

Figure 5 shows the electrical response of retinas to a single flash of bright light. A retina from three different mice were tested: a normal mouse (Figure 5A), a mutant mouse lacking the *Cnga3* gene (Figure 5B) and a mutant mouse lacking the *Cnga3* gene, but treated with 3 $\mu$ L of 1E12 vg/mL AAV-CNGA3 (Figure 5C). A high degree of restoration of function of mutant cones was observed in the retina from the *Cnga3* mutant mouse treated with AAV-CNGA3, with approximately 60% of the electrical response to a bright flash of light of the normal retina observed in the retina from the *Cnga3* mutant mouse that were treated with AAV-CNGA3. The mice were injected with AAV-CNGA3 at four weeks of age and assessed using ERG four weeks post injection.



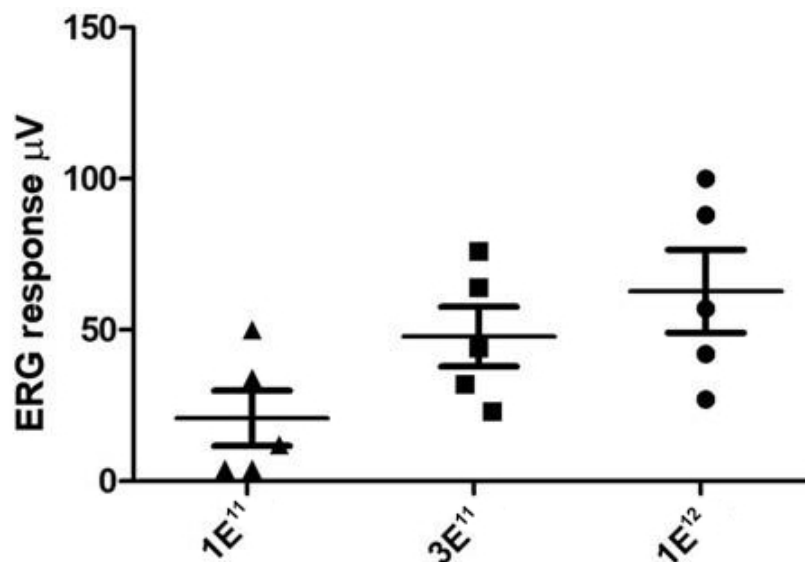
**Figure 5.** Cone electrical response in mice retinas reacting to a single flash of bright light, measured by ERG.

**Figure 5A.** The electrical response of the retina from a normal mouse reacting to a flash of bright light.

**Figure 5B.** The electrical response of the retina from a mutant mouse lacking *Cnga3* reacting to a flash of bright light.

**Figure 5C.** The electrical response of the retina from a mutant mouse lacking *Cnga3* treated with AAV-CNGA3 reacting to a flash of bright light.

Figure 6 shows the cone-mediated ERG responses measured in *Cnga3* mutant mice treated with three different doses of AAV-CNGA3. 3 $\mu$ L of AAV-CNGA3 was administered via subretinal injection in each eye at 1E11 vg/mL (n=5), 3E11 vg/mL (n=5) and 1E12 vg/mL (n=5). The mice were treated at 15 days old and the ERG was measured four weeks after treatment. The reviewer analyzing the ERG responses was masked to which eye received treatment. Doses tested in this study span the doses of AAV-CNGA3 proposed for our Phase 1/2 clinical trial. Figure 6 shows the ERG responses that were observed at each of the three doses.



**Figure 6.** The photopic ERG amplitudes measured to assess cone photoreceptor function in *Cnga3* mutant mice treated with AAV-CNGA3 at doses of 1E<sup>11</sup> vg/mL (n=5), 3E<sup>11</sup> vg/mL (n=5) and 1E<sup>12</sup> vg/mL (n=5). Mice were treated at 15 days post-natal and ERGs were assessed four weeks following treatment. The retinal ERGs are the electrical recordings corresponding to cone activity following a single pulse of bright light. A dose response was observed in retinal sensitivity obtained using the three tested doses and a treatment effect was also observed in the lowest dose tested.

In 2018, we anticipate completing a toxicology package similar to that used with the AAV-RPGR program using cGMP AAV-CNGA3 material manufactured at our cGMP facility. We anticipate conducting an approximately six month toxicology study in mice and two, eight week acute toxicology and biodistribution studies in mice and rabbits. The long-term toxicology study initiated in the first quarter of 2018.

#### *Clinical development of AAV-CNGA3*

We have an ongoing natural history study in ACHM including over 90 patients that allows us to collect structural and functional data for up to five years on prospectively defined endpoints, including functional tests (visual acuity, contrast sensitivity, mobility maze and photoaversion assessments), retinal imaging (color fundus photography, fundus autofluorescence imaging, spectral domain optical coherence tomography and visual field testing) and electrophysiological assessments. The study center is the Moorfields Eye Hospital in London. We believe access to these ACHM patients will enable us to efficiently enroll appropriate patients into our *CNGA3* Phase 1/2 clinical trial. In addition to giving us access to patients and potentially accelerated enrollment in our treatment study, we believe the prospective natural history data on each treated patient will allow us to gather robust data from our Phase 1/2 clinical trial in a condensed timeframe.

We aim to initiate a Phase 1/2 dose escalating trial of AAV-CNGA3 in ACHM patients with mutations in *CNGA3*. We expect this clinical trial will have the same design as our ongoing AAV-CNGB3 Phase 1/2 clinical trial and will initially be conducted in both adult and pediatric patients at two sites in the United States and Europe. AAV-CNGA3 clinical material is currently being manufactured at our cGMP facility. We expect to release material for this trial in early 2019 and open a Phase 1/2 dose escalation trial in *CNGA3* patients shortly thereafter.

## ***X-Linked Retinitis Pigmentosa***

### *Disease Background and Market Opportunity*

Retinitis pigmentosa, or RP, is a group of IRDs which represent the most common genetic cause of blindness. The condition is characterized by progressive retinal degeneration and vision loss that ends in complete blindness. There are currently no approved treatments for RP. We believe gene therapy is a promising therapeutic approach. RP initially presents as nighttime blindness during childhood or early adulthood, progressing to peripheral visual field loss and “tunnel vision,” central visual impairment, reduced visual acuity and, ultimately, complete blindness.

RP may be caused by mutations in any of over 100 different genes. The most severe forms of RP are X-linked, or XLRP, with onset in early childhood and rapid progression to blindness generally by the time patients reach 30 to 40 years old. RP has an estimated prevalence of one in 3,500 in the United States, and between 10% and 15% of RP patients are estimated to suffer from XLRP. The most frequent mutation causing XLRP is in the retinitis pigmentosa GTPase regulator gene, or *RPGR*. XLRP associated with a mutation in *RPGR*, or XLRP-*RPGR*, accounts for more than 70% of cases of XLRP. There are estimated to be approximately 20,000 XLRP-*RPGR* patients in the United States, Japan and EU5, with a little less than 50% those patients being under the age of 40 and approximately 200 new cases being diagnosed annually. We believe the availability of a therapeutic option may increase patient identification and the estimated prevalence of XLRP-*RPGR*.

The *RPGR* protein has an essential role in the maintenance of the structure and function of both rod and cone photoreceptors. The *RPGR* protein is tightly localized in the photoreceptors at the junction of the inner and outer segments, or cilium, of the photoreceptors. Correct localization of the *RPGR* protein to this site is important for the transport of light sensing proteins to the outer part of the photoreceptors, where these proteins convert light signals into electrical signals. In the absence of the *RPGR* protein the movement of light sensing protein within both rods and cones is impaired, leading to dysfunction and death of photoreceptors, resulting in retinal degeneration and ultimately complete blindness.

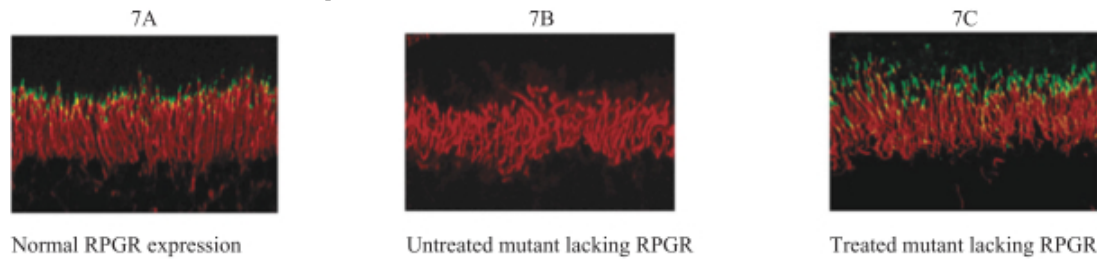
### *Our Gene Therapy Program*

Our product candidate for the treatment of XLRP, AAV-*RPGR*, is designed to treat XLRP caused by mutations in *RPGR*, the most common form of XLRP. The eye specific form of *RPGR* is encoded by a nucleotide sequence called *RPGR* open reading frame 15, or *RPGR-ORF 15*. Both rods and cones photoreceptors require *RPGR-ORF 15* to function. The protein coding message *RPGR-ORF 15* contains a region of repeated sequences that make the *RPGR-ORF 15* nucleotide sequence unstable in the cell. We have engineered a small deletion in *RPGR-ORF 15* that we observed was associated with a stable sequence that rescued *RPGR* protein levels, localization and function in mouse and human photoreceptors in preclinical studies. Our novel AAV-*RPGR* viral vector utilizes the human rhodopsin kinase, or *RK*, promoter to specifically drive the expression of our stabilized *RPGR-ORF 15* in both rods and cones. We selected the AAV5 capsid because of its efficient transfection into both of these types of photoreceptors.

In preclinical studies, performed at UCL IO between 2009 and 2015 and discussed in *Gene Therapy* in 2016, it was observed that treatment with AAV-*RPGR* containing our stabilized *RPGR-ORF15* was associated with rescue of the *Rpgr* mutant phenotype in mice that completely lacked the *RPGR* protein as measured by ERG responses of retinas from *Rpgr* mutant mice and assessments of *RPGR* protein. Restored levels, localization and function of *RPGR* protein in mutant mice lacking the *Rpgr* gene were observed, along with the restoration and localization of photosensitive proteins in both rod and cone photoreceptors, and reduction of long-term retinal degeneration. In addition to these experiments in *Rpgr* mutant mice, we have observed that our *RPGR-ORF 15* construct also rescued levels, localization and function of *RPGR* protein in human photoreceptors, in HMRs derived from patients with *RPGR* mutations. We believe that AAV-*RPGR* may have the potential to positively impact human photoreceptor function and survival in XLRP-*RPGR* patients, slowing or halting the degeneration that leads to blindness in these patients.

Figure 7 and Figure 8 show data from these preclinical studies regarding the effect of subretinal delivery of AAV-RPGR containing our stabilized *RPGR-ORF 15* in mice lacking the *Rpgr* gene. In these studies, different color stains were used to investigate the restoration of (i) RPGR protein expression, (ii) correct localization of RPGR protein and (iii) RPGR function. Figure 7 and Figure 8 show a retina from a normal mouse (7A and 8A), a retina from a mutant mouse strain lacking the gene for *Rpgr* (7B and 8B) and a retina from the same mutant mouse strain that lacks the gene for *Rpgr*, but treated with AAV-RPGR containing our stabilized *RPGR-ORF 15* (7C and 8C).

The red stain in Figure 7 marks a photoreceptor protein, rootletin, within the cilium, or middle section, of every photoreceptor, while the green stain reveals the localization of RPGR protein. The green stain in Figure 7A shows the localization of RPGR protein within the photoreceptor at the end of the cilium in a normal mouse retina. Figure 7B shows a retina from a mouse lacking the *Rpgr* gene without any green staining, indicating the absence of the RPGR protein. Figure 7C shows a retina from a mouse lacking the *Rpgr* gene that was treated with AAV-RPGR containing our stabilized *RPGR-ORF 15*. The green staining at the end of the photoreceptor cilium is similar to the normal mouse retina. Treatment with AAV-RPGR containing our stabilized *RPGR-ORF 15* was associated with the restoration of RPGR protein expression and localization within the individual photoreceptor cells consistent with normal RPGR expression.



**Figure 7.** In these preclinical mouse models, the red staining marks a normal protein in the photoreceptor cilia, rootletin, while the green stain reveals localization of RPGR protein within the photoreceptor.

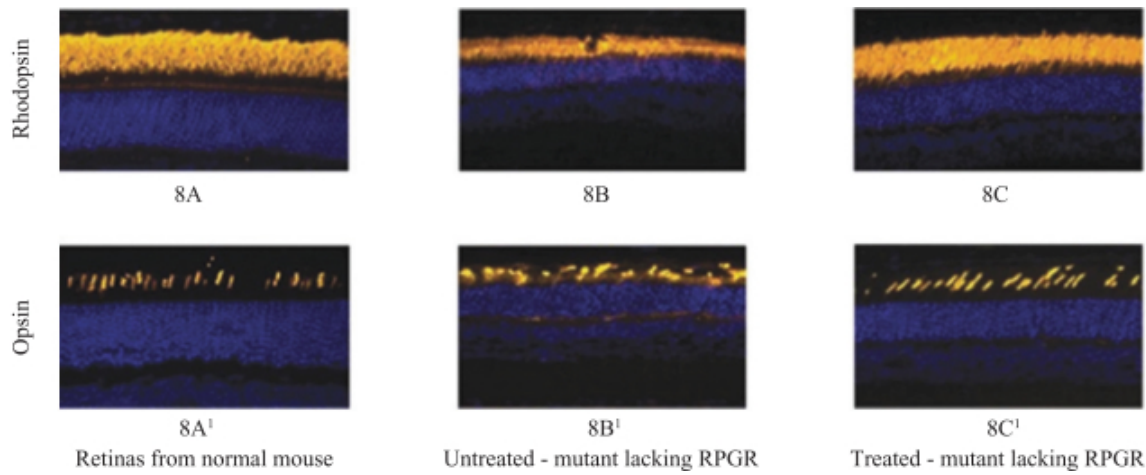
**Figure 7A.** The retina from a normal mouse.

**Figure 7B.** The retina from a mouse completely lacking the *Rpgr* gene.

**Figure 7C.** The retina from a mouse completely lacking the *Rpgr* gene and treated with AAV-RPGR containing our stabilized *RPGR-ORF 15*. The green stain indicates that RPGR protein expression was restored and was similarly localized within the individual photoreceptor consistent with normal RPGR expression.

Figure 8 shows a different analysis of retinas from the same mutant mouse strain that completely lacks the gene for *RPGR* expression. This analysis uses a yellow tag to reveal the location of photoreceptor light pigment, or opsins. The top row shows the rod opsin (8A; 8B; 8C), rhodopsin, and the bottom row shows cone opsin (8A'; 8B'; 8C'). Fully functional RPGR is critical for the correct localization of opsins and Figures 8B and 8B' show that in a *Rpgr* mutant mouse retina the opsins are incorrectly localized. Figures 8C and 8C' show that treatment of these mutant animals with subretinal injection of AAV-RPGR containing our stabilized *RPGR-ORF 15* enabled the correct location of the opsins within the photoreceptor as seen in the similarity to the normal mouse, indicating that RPGR is functionally active in supporting correct localization of key photoreceptor proteins.





**Figure 8.** In these preclinical mouse experiments, a yellow tag reveals the location of the opsins.

**Figures 8A and 8A'.** Normal mouse retina showing the localization of rhodopsin and opsin.

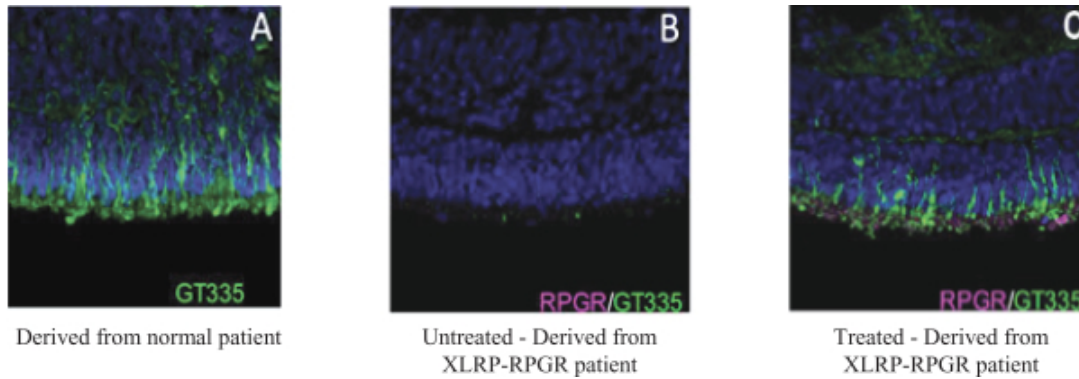
**Figures 8B and 8B'.** *Rpgr* mutant mouse retina showing the localization of rhodopsin and opsin.

**Figures 8C and 8C'.** *Rpgr* mutant mouse retina that was treated with AAV-RPGR containing our stabilized *RPGR-ORF 15* shows the localization of rhodopsin and opsin. The similar localization between the normal mouse retina and the *Rpgr* mutant mouse retina that was treated with AAV-RPGR containing our stabilized *RPGR-ORF 15* indicates that the rhodopsin and opsin are correctly localized and can perform their key function in the visual cycle.

We are further advancing the HMR system to evaluate the potential for our product candidates to functionally restore mutant photoreceptor cells in a human retina.

One of the many tasks that *RPGR* performs in the photoreceptor is to enable a process called glutamylation of a key cilia protein called tubulin, which is required for photoreceptor function. We conducted an *in vitro* study at UCL IO in 2016 using HMRs derived from stem cells from XLRP-RPGR patients to determine the effect of AAV-RPGR containing our stabilized *RPGR-ORF 15* on human photoreceptors. The data from this study has not been published. An HMR grown from hPSC from a normal individual is shown in Figure 9A, in which glutamylation of tubulin in normal human photoreceptors is stained in green. Figure 9B shows a HMR derived from a XLRP-RPGR patient and cultured over several months to form many of the anatomic layers of the retina and consisting of all photoreceptor types, while Figure 9C shows the impact of AAV-RPGR containing our stabilized *RPGR-ORF 15* treatment on a similarly cultured HMR derived from a XLRP-RPGR patient.

The HMR derived from a XLRP-RPGR patient lacks RPGR protein, making the photoreceptors dysfunctional with no glutamylation of tubulin present (Figure 9B). When HMRs from a XLRP-RPGR patient were treated with AAV-RPGR containing our stabilized *RPGR-ORF 15* we observed that glutamylation of tubulin returned (Figure 9C). We also stained HMRs derived from an XLRP-RPGR patient with a pink marker of RPGR protein. In Figure 9B no pink staining was observed, confirming the lack of RPGR protein. In Figure 9C, when the HMR from a XLRP-RPGR patient was treated with AAV-RPGR containing our stabilized *RPGR-ORF 15*, pink staining can be seen at the correct localization in the base of the cilium of the photoreceptors that are now stained with green glutamylation of tubulin marker. This restoration of RPGR protein expression and localization, and restoration of markers of photoreceptor function in human photoreceptors in HMRs derived from XLRP-RPGR patients, indicates potential clinical utility of AAV-RPGR containing our stabilized *RPGR-ORF 15*.



**Figure 9.** A HMR derived from hPSCs from a normal individual (9A) or a XLRP-RPGR patient (9B and 9C) cultured over several months to form many of the anatomic layers of the retina and consisting of all photoreceptor types with the glutamylation of tubulin having a green fluorescent stain.

**Figure 9A.** A HMR derived from normal hPSCs.

**Figure 9B.** A HMR derived from a XLRP-RPGR patient.

**Figure 9C.** A HMR derived from a XLRP-RPGR patient that was treated with AAV-RPGR containing our stabilized *RPGR-ORF 15*. The appearance of pink RPGR protein at the base of the photoreceptor cilium and glutamylation of tubulin returns, demonstrating the restoration of RPGR protein expression, localization and function.

To support the advancement of AAV-RPGR into clinical development, we conducted three single-dose toxicology studies from January 2016 to August 2017 at UCL IO. We performed a six month toxicology study in normal mice delivering doses of saline in both eyes for the control (n=5), and doses of AAV-RPGR in both eyes of  $2E^9$  vg/eye (n=5) and  $4E^9$  vg/eye (n=5), with a toxicology assessment at one, three and six months post-administration. Two further toxicology studies were performed. An eight week mouse study in which groups of mice were dosed with saline in both eyes as a control (n=15), AAV-RPGR in both eyes at  $1E^9$  vg/eye (n=15) or AAV-RPGR in both eyes at  $4E^9$  vg/eye (n=15), providing five mice from each group for studying local and systemic effects at each time-point of one, four and eight weeks after treatment. An eight week rabbit study was also conducted, in which nine right eyes were dosed per group, with doses of saline as a control, and AAV-RPGR doses of  $0.8E^{11}$  vg/eye and  $2.4E^{11}$  vg/eye, providing three rabbits for studying local and systemic effects at each time-point of one, four and eight weeks after treatment. Biodistribution was examined in the eight week mouse and rabbit studies. No harmful effects on the retina or systemically were observed. We used these data to support our CTA and IND for treatment of XLRP-RPGR patients with AAV-RPGR.

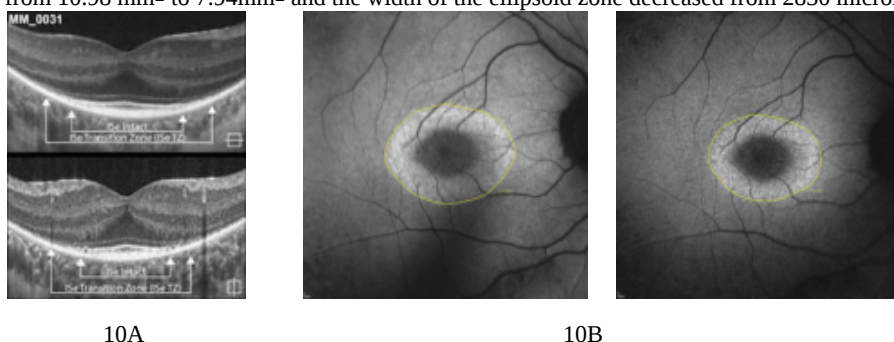
#### *Clinical Development of AAV-RPGR*

We have an ongoing natural history study in XLRP-RPGR including approximately 100 patients, which allows us to collect structural and functional data for up to five years on prospectively defined endpoints,

including functional tests (visual acuity and contrast sensitivity), retinal imaging (color fundus photography, fundus autofluorescence imaging, spectral domain optical coherence tomography, adaptive optics and visual field testing) and electrophysiological assessments. The study centers are the Moorfields Eye Hospital in London, the Kellogg Eye Center at the University of Michigan, the Medical College of Wisconsin & Froedtert Hospital and Massachusetts Eye and Ear. We believe access to this large population of XLRP-RPGR patients has enabled us to efficiently enroll appropriate patients into our XLRP-RPGR Phase 1/2 clinical trial. In addition to giving us access to patients and potentially accelerated enrollment in our treatment studies, we believe the prospective natural history data on each treated patient will allow us to gather robust data from our Phase 1/2 clinical trial in a condensed timeframe. Of particular interest is the area and width of the ellipsoid zone, which is a validated surrogate marker of retinal degeneration in RP and other IRDs.

The ellipsoid zone is a marker of retinal structure observed by optical coherence tomography, or OCT, and has been demonstrated to contract as the retina degenerates in a number of different IRDs. The ellipsoid zone has been shown to progressively decrease over time in step with the degeneration of the retina that occurs in XLRP-RPGR patients. Our natural history study provides data on ellipsoid zone width and area for up to five years prior to treatment with AAV-RPGR for each patient that then enrolls in our gene therapy treatment trial.

Figure 10 shows two sets of images taken 24 months apart using OCT and fundus autofluorescence imaging, two imaging techniques used to capture micrometer-resolution images of the eye, of the ellipsoid zone of one XLRP-RPGR patient in the natural history study. This patient was 20 years old upon entering the study when the first assessment was taken. Measurements associated with these images show that the ellipsoid zone area decreased from 10.98 mm<sup>2</sup> to 7.94mm<sup>2</sup> and the width of the ellipsoid zone decreased from 2830 microns to 2204 microns over 24 months.



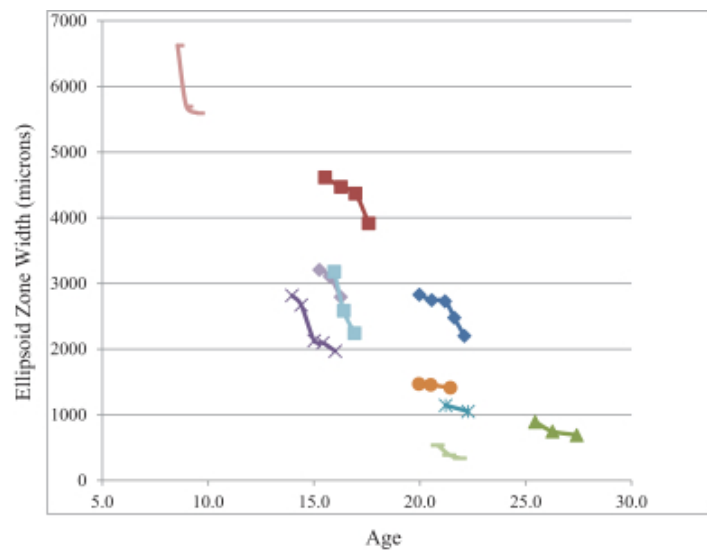
**Figure 10.** OCT and fundus autofluorescence images of the ellipsoid zone of one RPGR-XLRP patient in the natural history study taken 24 months apart. During the 24 month time frame the width and area of the ellipsoid zone have diminished.

**Figure 10A.** These two OCT images, taken 24 months apart at the same position in the retina, illustrates the width of the ellipsoid zone.

**Figure 10B.** These two images show the fundus autofluorescence imaging of the same retina taken 24 months apart. The fovea is located approximately in the center of the ring and can be seen as a slightly darker dot. The outlined “autofluorescent” area was reduced over the 24 months between the capture of the two images.

A further benefit of the XLRP-RPGR natural history study is access to longitudinal data from the population of XLRP-RPGR patients over time. Figure 11 is a graph of data collected in our XLRP-RPGR natural history study of individual patients, which evidence a relationship between a patient’s ellipsoid zone width and age. These data show a reduction in ellipsoid zone width over time in each patient, as well as the increased rate of

decline in younger individuals. We believe these data will support both our Phase 1/2 clinical trial and any future pivotal trial by enabling us to select patients with similar characteristics and rate of disease progression for treatment with AAV-RPGR, as well as providing longitudinal and individual patient data on the rate of ellipsoid zone shrinkage to more readily assess the impact of therapeutic intervention.



**Figure 11.** Graph of data gathered in our XLRP-RPGR natural history study showing the correlation between ellipsoid zone width (Y-axis) and age (X-axis) in individual patients.

We are conducting a Phase 1/2 clinical trial of AAV-RPGR in both adult and pediatric XLRP-RPGR patients. This trial is open in the United Kingdom under our CTA and United States under our IND. In the dose escalation phase of the trial, up to 18 adult patients may be administered one of three different doses of vector in dose escalating cohorts of three to six patients at a time. Once an acceptable safety profile has been established in adults, up to 18 children may then be treated at an acceptable dose. The primary endpoint of this open-label, dose-escalation clinical trial is the safety of delivering AAV-RPGR through subretinal injection. Secondary endpoints include the outcomes of a range of functional tests, quality of life measures and detailed analysis of the retina, including structural analysis of individual photoreceptors and measurements of ellipsoid zone via optical coherence tomography and fundus autofluorescence ring size. Following discussions with the FDA, we will be splitting the pediatric extension cohort into two groups to be treated with two different doses of AAV-RPGR. We will look at a range of functional and structural assessments including the ellipsoid zone progression as an acceptable surrogate marker of retinal degeneration with the aim of gaining early data on the activity of our potential gene therapy product in this patient population. Retinal images of treated and untreated fellow eyes at different time-points will be read at an independent reading center and evaluators will be blinded to treatment.

RP initially presents as nighttime blindness during childhood or early adulthood, progressing to peripheral visual field loss and “tunnel vision,” central visual impairment, reduced visual acuity and, ultimately, complete blindness. XLRP-RPGR is a progressive disease in which the retina gradually degenerates starting in the outer, or peripheral, regions of the retina and initially causing “tunnel vision” with final degeneration of the central retina resulting in the complete loss of visual acuity and blindness that generally occurs by the time patients are 30 to 40 years old. We believe that to prevent this ultimate degeneration to blindness and to retain visual acuity, the central region of the retina, including the macula and fovea, must be preserved. To this end, we aim to deliver AAV-RPGR to this central region of the retina. In our Phase 1/2 clinical trial, AAV-RPGR viral vector is delivered via subretinal injection of up to 1mL with the potential for the surgeon to use multiple

retinotomies targeting the region of the central retina, including the macula and fovea. One eye is treated in each patient, which is the eye assessed to be the worst eye at baseline.

We have treated six adult (aged 19 to 30 years old) patients in the Phase 1/2 XLRP-RPGR clinical trial, three patients in cohort one at a dose of  $1E^{11}$  vg/ml and three patients in cohort two at a dose of  $2E^{11}$ vg/ml. In all patients, subretinal injection covered the central part of the retina, including the macula and fovea. Following review of the safety data from cohort one of this trial, the IDMC recommended escalation of dose in the second cohort.

As of May 4, 2018, we have three month data on the three patients in cohort one, with one patient reaching six months post treatment. While preliminary, we observed indications of improved retinal sensitivity in the first two patients in cohort one as assessed by two different measures of retinal sensitivity, navigation of the mobility maze in dim lighting conditions and perimetry using the Octopus 900 perimeter to assess the sensitivity of the central retinal field. The Octopus 900 perimeter assesses light sensitivity across the retinal field by measuring patients response to small spots of light in a grid. In both of these patients, data from Octopus 900 perimetry assessments compared to baseline measurements showed signs of improvement in retinal sensitivity at three months following treatment, with continued signs of improvement in the first patient to reach the six month post-treatment assessment. In both patients we also observed improvement in the speed and error rate of navigating the mobility maze at low light levels (one lux) at the three month assessment following treatment compared to pretreatment baseline in the treated eye and not in the untreated eye. This early signal of improvement in two assessments of photoreceptor function in XLRP-RPGR patients following treatment with AAV-RPGR is encouraging. However, this is preliminary data and needs to be supported by data collected at later time-points and in larger numbers of patients in future cohorts.

We anticipate completing adult dosing in this Phase 1/2 clinical trial during the third quarter of 2018, and completing the dosing of the two pediatric cohorts in 2019.

We will close out this trial 18 months after the last pediatric patient has been treated. Patients will then move into a long-term follow up study for safety and indication of benefit for an additional three and a half years.

The FDA and EMA have granted orphan status to AAV-RPGR for the treatment of retinitis pigmentosa. The FDA has also granted fast track designation to AAV-RPGR for the treatment of XLRP caused by defects in *RPGR*.

## ***RPE65-Deficiency***

### *Disease Background and Market Opportunity*

*RPE65*-deficiency causes rod photoreceptor dysfunction and impaired vision from birth. The *RPE65* gene encodes a protein that is produced in the retinal pigment epithelium, or RPE, a thin layer of cells at the back of the eye that support photoreceptors and nourish the retina. The *RPE65* protein is essential for rod function because it recycles the light sensing machinery in rod photoreceptors. Absence of *RPE65* results in severe dysfunction of rods and causes impaired vision in dim lighting conditions. Although cone photoreceptors are generally preserved during childhood in *RPE65*-deficient patients, the lack of function and degeneration of the rods eventually results in the loss of cones and degeneration of the whole retina over time. Consequently, most *RPE65*-deficient patients experience central vision loss progressing to complete blindness by early adulthood.

*RPE65*-deficiency is often characterized as a specific subtype of Leber congenital amaurosis or RP that is caused by mutations in the *RPE65* gene, called Leber congenital amaurosis 2 and RP20, respectively. However, we believe a more precise approach to genetic diseases is to focus on the underlying genetic defect, rather than the phenotype, and have therefore identified *RPE65*-deficiency as the target of our product candidate AAV-RPE65.

Based on an estimated prevalence of approximately one in 500,000 people in the United States suffering from Leber congenital amaurosis, or LCA, related to mutations in the *RPE65* gene, and approximately one in 70,000 people in the United States having RP due to mutations in the *RPE65* gene, *RPE65*-deficiency occurs in approximately one in 125,000 people in the United States. There are estimated to be approximately 6,000 *RPE65*-deficiency patients in the United States, Japan and EU5, with almost 30% of those patients being under the age of 30 and approximately 50 new cases being diagnosed annually. We believe the availability of a therapeutic option may increase patient identification and estimated prevalence of *RPE65*-deficiency.

### Our Gene Therapy Program

Our gene therapy candidate for the treatment of *RPE65*-deficiency, AAV-RPE65, is an AAV2/5 viral vector, in which a codon optimized *RPE65* gene is driven by a novel synthetic RPE cell specific promoter.

*RPE65*-deficiency is a well validated condition for gene replacement therapy. In multiple clinical trials, including one conducted by our collaborators at UCL, replacing the mutant *RPE65* gene with a normal copy of the gene resulted in improved nighttime vision in affected children and young adults, suggesting the potential impact of gene therapy on rod function in this disease. The FDA recently approved the first gene treatment for *RPE65*-deficiency, Luxturna. While *RPE65*-deficiency primarily causes a loss of rod function initially leading to impaired vision in dim light, these patients ultimately experience complete blindness because of degeneration of the cone rich fovea. To prevent blindness, therefore, we believe it is critical to treat the central retina in order to maintain structural integrity in this region and save central vision. We aim to treat as extensive an area of the central retina as possible, including the cone rich fovea. Thus, in addition to improving rod function, we aim to provide sufficient RPE65 protein to the cells in the central retina to prevent the degeneration of both rods and cones in this region, and thereby prevent the progression to complete blindness.

We focus on detailed structural and functional data in our treatment studies with the aim of demonstrating an impact on the degeneration of the central retina.

Our novel AAV2/5 vector, AAV-RPE65, has been optimized for both transduction of RPE cells and RPE65 protein production and our surgical approach targets the central area of retina whose preservation is most critical for long term maintenance of visual function. Building on the work of Professor Ali and in collaboration with the team at UCL, we have developed AAV-RPE65. AAV-RPE65 is a second generation viral vector that has compared favorably to our first generation AAV2/2 vector in a number of ways, including being two to three logs, or 100 to 1,000 times, more potent on a particle for particle basis than our original AAV2/2 vector in a head to head *Rpe65* null animal model rescue experiment. On a logarithmic scale, each “log” represents a 10-fold change. We believe this increased potency will improve transgene expression and RPE65 protein production in the back of the eye. The table below summarizes elements of the optimization of AAV-RPE65 compared to our original AAV2/2 vector. Vector optimization studies were performed at UCL IO and were carried out from 2010 to 2015. The data summarized here was referred to in *Gene Therapy* in 2016. We used these data to support our IND and CTA for treatment of *RPE65*-deficient patients with AAV-RPE65.

Optimization of AAV2/5 compared to AAV2/2	
Transfection Efficiency	Changing the capsid from AAV2/2 to AAV2/5 was associated with an improvement of the transfection efficiency of RPE by four times.
Protein Expression (Promoter)	AAV2/5's optimized promoter was associated with a 20 times increase in protein expression.
Protein Expression (Codon)	AAV2/5's optimized codon usage was associated with a seven times increase in protein expression in human cells.
mRNA Stability	Utilizing SV40 intron increases mRNA stability and was associated with a two and one half times increase in protein production.
Overall Efficacy	The optimized construct was associated with a 300 to 1,000 times increase in efficacy in mouse functional rescue and is expected to be two to three logs more potent on a particle for particle basis in humans.

We conducted four single-dose toxicology and biodistribution studies of AAV-RPE65 from January 2015 to December 2016. We performed a long-term toxicology study in normal mice in which four eyes were

dosed with saline as a control and nine eyes were dosed with AAV-RPE65 at  $4E^9$  vg/eye, with a toxicology assessment at one, three, six and nine months post-administration. We also conducted an eight week mouse study, an eight week rabbit study and an eight week minipig study. In the mouse study, 15 mice were dosed in both eyes with saline as a control, 15 mice were dosed in both eyes with AAV-RPE65 at  $1.2E^9$  vg/eye and 15 mice were dosed in both eyes with AAV-RPE65 at  $3.7E^9$  vg/eye, providing five mice from each group for studying local and systemic effects at each time-point of one, four and eight weeks after treatment. In the rabbit study, nine rabbit's right eyes were dosed for each group with a saline control group, a  $0.6E^{11}$  vg/eye group and a  $1.9E^{11}$  vg/eye group, providing three animals from each group for studying local and systemic effects at each time-point of one, four and eight weeks after treatment. The minipig study was a two week single dose injection study in minipigs (n=2, each dosed in one eye) at a dose of  $1.84E^{10}$  vg/eye. The minipig study was performed by Charles River Laboratories, while the other three studies were performed at UCL IO. No harmful effects on the retina were observed during these studies. We used these data in support of our CTA and IND for treatment of RPE65-deficient patients with AAV-RPE65.

### *Clinical development of AAV-RPE65*

We have an ongoing natural history study in patients with RPE65-deficiency with approximately 30 patients enrolled that allows us to collect structural and functional data on prospectively defined endpoints, including functional tests (mobility maze, color vision, visual acuity and quality of life measures), retinal imaging (color fundus photography, fundus autofluorescence imaging, visual field testing, spectral domain optical coherence tomography and adaptive optics) and electrophysiological assessments. The study is global, with study centers including at the Moorfields Eye Hospital in London, University of Michigan Kellogg Eye Center and the Medical College of Wisconsin & Froedtert Hospital. We plan to present this natural history data to regulatory agencies in our meetings following completion of the Phase 1/2 clinical trial for discussion of our pivotal trial design and path to regulatory approval.

A Phase 1/2 clinical trial of AAV-RPE65 in both adult and pediatric patients is ongoing. The design of the trial is the same as our ACHM Phase 1/2 clinical trials. In the dose escalation phase of the trial, up to 18 adult participants may be administered one of three different doses of vector in dose escalating cohorts of three to six participants at a time. Once an acceptable safety profile has been established in adults, up to nine children may then be treated at an acceptable dose. The primary endpoint of this open-label, dose-escalation clinical trial is the safety of delivering AAV-RPE65 through subretinal injection in patients with RPE65-deficiency. Secondary endpoints include the outcomes of a range of functional tests, detailed structural analysis of the retina and quality of life measures.

This clinical trial is enrolling patients in the United Kingdom under our CTA, as well as the United States under our IND. We have treated 14 patients in this clinical trial and the first seven patients have consented to participate in the long-term follow up study. Children are currently being dosed in the United States and United Kingdom. Surgeries in this trial have been carried out in the United States at the University of Michigan Kellogg Eye Center and in the United Kingdom at the Moorfields Eye Hospital by three different surgeons. No differences in outcomes have been observed between the different surgeons.

In cohort one, three adults (aged 19, 20 and 20 years old) were administered up to 1mL of  $1E^{11}$  vg/mL of AAV-RPE65 vector. In each patient, the central region of the retina was targeted. No serious adverse events or dose limiting events have been reported in this cohort as of the 18 month time point following vector administration.

In each patient treated in cohort one, we observed improvement or stability in central visual function following treatment compared to baseline and compared to the untreated fellow eye. Retinal sensitivity was measured with threshold static perimetry using Octopus 900 perimetry and visual field modelling and analysis, or VFMA. Observations at 18 months following vector administration in the first cohort have demonstrated a

potential increase in retinal sensitivity by up to 40% from baseline. In contrast, we observed that the untreated eyes of patients in this cohort suffered a reduction in retinal sensitivity of up to 40%, which is consistent with data from our parallel prospective natural history study of *RPE65*-deficient patients. In addition to the perimetry and VFMA data, improvements in time and error rate in mobility maze navigation have been observed in these patients at six and 12 months following treatment. However, this is preliminary data and needs to be supported by data collected at later time-points and in larger numbers of patients.

In addition to the functional data discussed above, we are collecting detailed structural data on all patients in our Phase 1/2 clinical trial. This includes data to visualize the mosaic of individual cones in the central part of the retina over time in each patient. We have sequential cone map data for more than 18 months following subretinal injections that covered the macula and fovea in the patients in cohort one, and as of May 4, 2018, we have not observed retinal thinning or loss of cones over time following treatment. We are continuing to monitor the detailed structure of both treated and untreated fellow eye in the five year follow on study to assess if AAV-RPE65 treatment has an impact on degeneration in the treated area of the eye compared to the untreated fellow eye.

In cohort two, three adults (aged 16, 20 and 22) were administered vector peripherally via subretinal injection into the outer region of the retina at a higher dose of up to 1mL of  $3E^{11}$  vg/mL. Following completion of the four week steroid taper, in two patients inflammatory responses were noted by the investigator as being probably related to vector administration. Both responded to a further course of steroids. Improvements in visual mobility in study eye over non-study eye were observed at 12 months at the four lux lighting level in this cohort. Similar increases in retinal sensitivity to cohort one have not been observed at this dose level. We believe data from cohort two is suggestive that peripheral administration of the vector into more degenerating areas of the retina may result in an increased chance of an immune response with a decreased potential benefit compared central administration of the vector. Following the review of the safety data for each adult cohort treated in this study, the IDMC recommended escalation to the higher dose in the next cohort.

Based on the safety and activity data from the patients treated at the  $1E^{11}$  vg/mL dose level (cohort one), the decision was made to treat pediatric patients at this dose prior to receiving the full safety data from adult cohort three, and to target the central part of the retina in all pediatric patients. Treatment of pediatric patients is currently ongoing in the United Kingdom and United States and five pediatric patients have been treated. We expect to treat one additional pediatric patient in this trial.

We carry out detailed assessments of retinal sensitivity across the entire retina, with the majority of tested retinal locations covering the central retina, at baseline and at prospectively defined time-points following treatment using the Octopus 900 perimeter. The Octopus 900 perimeter, unlike other standard clinical devices, enables full-field static perimetry using testing algorithms specifically designed for retinal conditions, affords the use of custom-developed testing grids, and allows the full dataset to be extracted and modelled for more accurate measurement of change over time.

Discreet small spots of light are shone onto multiple predetermined points (the test grid) covering the central retinal field and peripheral retina, with the patient responding each time they perceive a spot of light. Each point on the retina is tested multiple times with different intensities of light, thereby allowing the determination of both the reliability and reproducibility of the patients' response to each light level at each spot and an accurate measurement of the exact retinal sensitivity at topographically determined points. The data is read out as a 'heat map' of sensitivity across the retinal field. The reliability of the patient and the data produced is also calculated and provided by the machine. In addition to the heat map of retinal sensitivity and conventional mean sensitivity metric produced by Octopus 900 assessment, we also conduct advanced VFMA. This produces a volumetric measure of retinal sensitivity presented both numerically as well as in a topographical retinal sensitivity map, which better represents the entire dataset across the visual field. We compare the VFMA data from the retinal map at each timepoint following treatment to the baseline data to measure the extent and position of changes in retinal sensitivity over time in treated and untreated eyes.

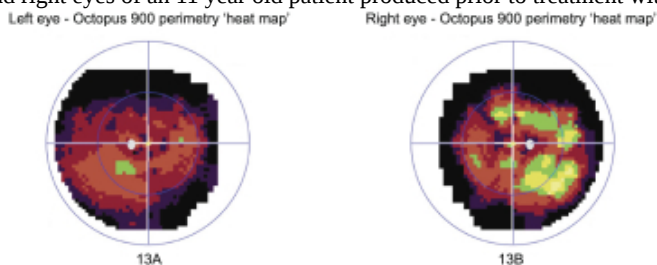


As of May 4, 2018, we have received initial post-treatment Octopus 900 perimetry data in which we observed a strong response at the three month time-point in an 11 year old pediatric patient treated with AAV-RPE65 at a dose of  $1E^{11}$  vg/mL, one of the two pediatric patients we currently have follow up data from that time point on. However, this is preliminary data and needs to be supported by data collected at later time-points and in larger numbers of patients. Figure 12 shows the 'heat maps' produced by Octopus 900 assessment showing the light sensitivity across the retinal fields of the left (Figure 12A) and right (Figure 12B) eyes of this 11 year old RPE65 patient at baseline prior to treatment with AAV-RPE65. Figure 13 shows the 'heat maps' produced by Octopus 900 assessment showing the light sensitivity across the retinal fields the untreated left eye (Figure 13A) and the treated right eye (Figure 13B) of this 11 year old RPE65 patient at the first Octopus 900 assessment at three months following treatment with AAV-RE65 at a dose of  $1E^{11}$  vg/mL via subretinal injection covering the central retina including the macula and fovea.

The increased color observed in the patient's right eye in Figure 13 compared to the right eye in Figure 12, and especially the prominence of the green and yellow in the right eye, indicates a significant increase in light sensitivity in these areas of the retina. The reliability of this patient's data measured by the Octopus 900 perimeter scored the highest level achievable in the test. Reliability scores measured by Octopus 900 range from zero to 100, with 100 being totally unreliable and zero being the maximum reliability score. This patient achieved a reliability score of zero.



**Figure 12.** Image of the 'heat map' left and right eyes of an 11 year old patient produced prior to treatment with AAV-RPE65.



**Figure 13.** Image of the heat map left and right eyes of an 11 year old patient produced three months following treatment with AAV-RPE65 in the right eye, the left eye was untreated.

We anticipate completing dosing of the final pediatric patients in the second half of 2018. We will close out this trial six months after the last pediatric patient has been treated. Patients will then move into a long term follow up study in which patients will be followed for safety and an indication of benefit for an additional four and a half years.

Preliminary six month data from the full pediatric cohort will be available in the first half of 2019, along with top line data from the adults treated in the dose escalation phase of this study.

The FDA and EMA each granted orphan status to AAV-RPE65 for the treatment of LCA caused by mutations in *RPE65*. The FDA also granted AAV-RPE65 rare pediatric disease designation for the treatment of inherited retinal dystrophy due to biallelic *RPE65* mutations.

## **LCA4**

### *Disease Background*

LCA4 is an IRD that causes complete blindness before age five. *AIPL1* is a central protein for the maintenance of photoreceptor structure and function. Deletion of the *AIPL1* gene causes the most severe form of early retinal dystrophy, LCA4, in which the retinal structure is destroyed with complete vision loss. LCA4 is rare, representing approximately 8% of all LCA cases.

There are currently no approved treatments for LCA4, and we believe an effective intervention will require introducing a normal functional copy of the *AIPL1* gene into rod and cone photoreceptors early in a patient's life while some retinal structure remains in order to activate function and survival of the photoreceptors that are still present. We believe gene therapy has the potential to be the only effective way to address the disease's root cause.

### *Our Gene Therapy Program*

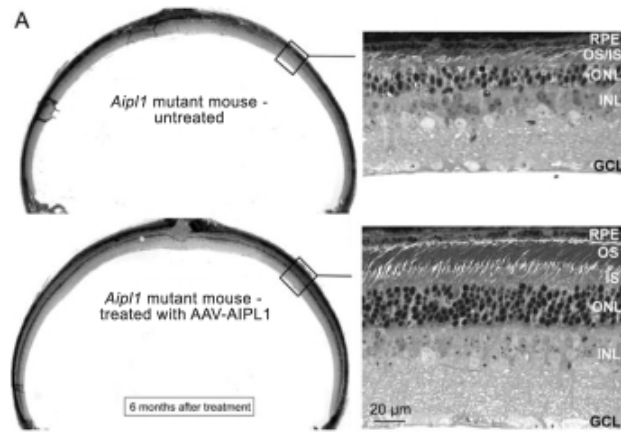
LCA4's extremely rapid progression, rarity and early age of onset make the standard process of seeking regulatory approval through clinical development challenging because adult safety trials would not yield meaningful data given the early onset of the disease. We believe we are well placed to initiate the first clinical intervention in this indication through our relationships with UCL and Moorfields Eye Hospital, whose expertise and large IRD patient population enables such an aggressive and uncommon IRD to be treated.

To address LCA4, we developed a viral vector to replace the *AIPL1* gene in all photoreceptors by using the *AIPL1* cDNA driven by the rhodopsin kinase promoter, which is active in both rods and cones.

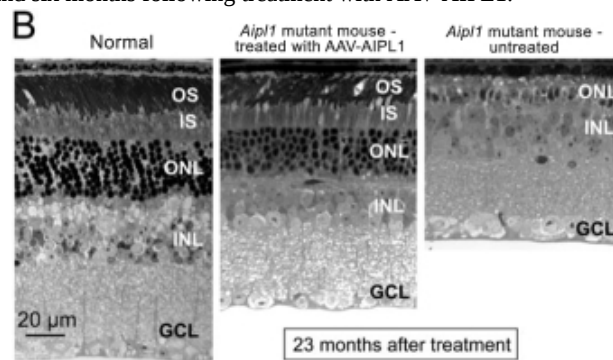
Much of the preclinical work to support the proof of concept for gene therapy in LCA4 was conducted by our collaborators at UCL IO, led by Professor Robin Ali, and was published in *Gene Therapy* in 2010.

Figure 14 and Figure 15 show histological sections revealing the structure of retinas from *Aipl1* mutant mice treated with AAV-AIPL1, compared to untreated retinas from *Aipl1* mutant mice, at six months and 23 months after treatment.

It was observed at both time-points that *Aipl1* mutant mice treated with AAV-AIPL1 suffered less photoreceptor loss than untreated *Aipl1* mutant mice, with the retinas of untreated mutant mice almost completely degenerated by 24 months of age. *Aipl1* mutant mice were treated with .5uL of AAV-AIPL1 at  $1E^{12}$  at four weeks post-natal and eyes were sectioned at six months and 23 months after treatment. These treated retinas were compared to retinas from untreated control *Aipl1* mice (n=17 eyes), and retinas from normal mice without the *Aipl1* mutation sectioned at the same post-natal ages as the treated *Aipl1* mutant mice. The data indicates that subretinal administration of AAV-AIPL1 is associated with the protection of the retina from degradation that occurs in *Aipl1* mutant mice, and this effect was durable out to two years, the oldest age studied in these mice.



**Figure 14.** Histological sections of retinas of *Aipl1* mutant mice treated with AAV-AIPL1 six months after treatment with AAV-AIPL1, compared to untreated retina. The top image is the retina of an untreated *Aipl1* mutant mouse at seven months post-natal. The lower image is the retina of a *Aipl1* mutant mouse at seven months post-natal, and six months following treatment with AAV-AIPL1.



**Figure 15.** Histological sections of retinas of *Aipl1* mutant mice treated with AAV-AIPL1 23 months after treatment with AAV-AIPL1, compared to untreated retina and retina from a normal mouse. The left image is the retina of a normal mouse at 24 months post-natal. The middle image is the retina of an *Aipl1* mutant mouse at 24 months post-natal, and 23 months following treatment with AAV-AIPL1. The right image is the retina of an untreated *Aipl1* mutant mouse at 24 months post-natal.

Clinical material was manufactured to cGMP standards under a special license. Some of this clinical material was used in studies in 2017 at UCL to confirm potency in an AIPL1 deficient mouse and to perform toxicology testing in normal mice and rabbits. A potency study was conducted at a AAV-AIPL1 dose of  $3 \times 10^9$  vg/eye with a group size of three eyes. Assessments were performed at three weeks and supported the potency of the cGMP clinical material through analysis of the ERG response.

A toxicology study was performed with normal mice and rabbits. In the mouse portion, five animals per group were evaluated for local and systemic effects at four weeks. In the rabbit portion, three animals per group were evaluated for local and systemic effects at four and eight weeks. Safety evaluation included functional assessments using ERG, funduscopy, and structural assessments.

Our product candidate, AAV-AIPL1, was manufactured and released for compassionate use under a special license in the UK to treat LCA4 patients at the Moorfields Eye Hospital. The UK's Human Medicines

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Regulations 2012 allow for the manufacture and supply of medicinal products not authorized for marketing to patients with special needs at the request of the healthcare professional responsible for the patient's care (these products are referred to as "specials"). A special may only be supplied in: (i) response to an unsolicited order from a healthcare professional responsible for the care of the patient, (ii) if the product is manufactured and assembled in accordance with the specifications of that healthcare professional to fulfil the special needs of the individual patient that cannot be met by products already authorized for marketing and (iii) if the product is manufactured under a specials license granted by the UK's Medicines and Healthcare Products Regulatory Agency, or MHRA.

The FDA and EMA granted orphan designation to our product candidate, AAV-AIPL1, for treatment of inherited retina dystrophy due to defects in *AIPL1* gene.

### ***Age-Related Macular Degeneration (AMD)***

#### Disease Background and Market Opportunity

AMD is a chronic eye condition that causes gradual decline of central vision. It is the leading cause of vision loss in individuals more than fifty years old in the United States and it affects 6.2 million people globally. Although AMD does not usually lead to complete blindness because peripheral vision is generally maintained, losing central vision has a critical impact on visual acuity, which is achieved by the closely packed cones of the central retina. As a result, loss of central retinal function has a significant impact on a person's independence and quality of life.

AMD is a complex disease attributed to several different causes. A number of genetic and environmental risk factors have been associated with the development of AMD. Two late forms of AMD have been characterized: geographic atrophy, or dry AMD, and neovascular AMD, or wet AMD. Dry AMD is characterized by the progressive, irreversible loss of many of the cell types in the retina, including the RPE, photoreceptors, and underlying capillaries of the macula, and causes a decline in central visual function. Wet AMD is defined by the growth and invasion of immature blood vessels from the underlying choroid into the retina. Leakage from these fragile blood vessels causes build-up of blood and fluid under the retina, leading to detachment of the RPE or retina and long term scarring.

Current therapeutic options for AMD are limited. There is no approved therapy that impacts the disease progression of dry AMD. The best available treatment for patients after they lose central vision and acuity is support and rehabilitation services to help them better utilize the remaining peripheral part of their retina.

Effective treatments for wet AMD are focused on blocking blood vessel growth, or angiogenesis, that underlies the pathology of the disease. These wet AMD treatments specifically block the activity of vascular endothelial growth factor, or VEGF, one of the key drivers of angiogenesis. There are two approved anti-VEGF treatments on the market, ranibizumab, or Lucentis, and aflibercept, or Eyelea. These may be effective in some wet AMD patients, but require challenging dosing regimens that typically include intra-ocular injections every one to three months.

### **Our Gene Therapy Programs**

#### *Wet AMD*

We aim to use a gene-based strategy to deliver an anti-angiogenic molecule to the retina and create a "local factory" that will deliver a continual supply of antiangiogenic molecules to the key parts of the eye. This would require a one-time injection procedure to deliver the gene therapy to the affected eye. We focus our blockade on the receptor involved in driving aberrant blood vessel growth and leakage, VEGF Receptor 2, or VEGFR2. Rather than depleting the VEGF ligand from the system we aim to block the receptor for that ligand

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preventing VEGF binding to the receptor and thereby preventing downstream pathology of wet AMD that is normally triggered by VEGF binding to VEGFR2. We use an anti-VEGFR2 antibody. In some rodent models the inhibition of the VEGFR2 with this antibody appears to have reduced long term toxicity as compared to the depletion of the VEGF ligand. Initial studies have identified a lead candidate that we have now moved from the research stage to formal preclinical development. We are also working to integrate our gene regulation technology with our wet AMD program. Our ultimate aim is to activate the anti-VEGFR2 antibody gene that we have installed in the eye with a small molecule applied topically with an eye drop. This could potentially allow for intermittent dosing of the antibody using an eye drop rather than an injection.

### *Dry AMD - Rod to Cone Program*

To treat dry AMD, and specifically to treat patients with geographic atrophy in which the central part of the retina is irreversibly damaged, we are advancing a novel strategy to alter the very character of rod photoreceptors.

In advanced forms of dry AMD, central visual function is lost after the fovea and the larger central retina area has degenerated, and any residual vision is generally via the outer retina's rods. A critical characteristic of cones that allows for response to high light levels is that they recover rapidly after they are stimulated by light. In contrast to cones, rods work in low light levels and require longer exposure to trigger an impulse and are then much slower to recover to a state when they can respond again. Therefore, seeing via rods is slow and imprecise, whereas cones mediate acute high resolution vision. By genetically engineering rods with molecules that will improve their speed of recovery and response to light, we aim to effectively transform a patch of rod photoreceptors to behave more like cones. This rod-to-cone transformation would potentially be achieved by using localized gene therapy vector placement in the rod-rich peripheral retina to create a small patch or "pseudo fovea," where cone like behavior of rods would enable the patient's brain to fixate on a functional part of the peripheral retina and recover a more cone like response to higher light levels.

The proof of concept has already been achieved in animal models, with first generation molecules designed to speed up the visual cycle recovery times in rods. We will continue to develop and optimize these molecules using our screening systems to allow selection for sensitivity to natural high light intensities and for the high refresh rate required.

### *Xerostomia*

#### *Disease Background and Market Opportunity—RIX*

Radiation induced xerostomia, or RIX, is a severe and debilitating long-term side effect of radiation treatment for head and neck cancer. There is not currently any FDA approved treatment for RIX. Worldwide, there are approximately 500,000 new cases of head and neck cancer diagnosed each year, with approximately 50,000 cases in the United States alone, making it the fifth most common malignancy. Approximately 85% of patients who receive radiation treatment for head and neck cancer experience reduced saliva production during treatment, and approximately 40% of those patients who remain cancer free for two or more years after treatment continue to suffer from grade 2 or 3 RIX. There are approximately 170,000 such patients in the United States, with approximately 10,000 new cases each year. Severity of RIX is measured from grade 1 (mildest) to 4 (most severe). As these patients tend to be under the care of a physician and dentist and have access to some form of health insurance, we believe this is an accessible indication with much larger commercial potential than some genetic diseases that are currently targets of our gene therapy programs.

RIX is a frequent side effect of head and neck cancer treatment because the standard treatment of locally advanced head and neck cancer involves radiotherapy, which can cause irreversible damage to non-diseased tissues located near oral tumors, such as the salivary glands. The fluid secreting, or acinar cells, of the salivary glands are uniquely sensitive to radiation, are destroyed acutely on IR exposure and to a large extent do not regenerate, resulting in chronically reduced salivary output. Because saliva plays such a critical role in the

physiology and protection of upper gastrointestinal, or GI, tract tissues, patients with chronic RIX suffer severe long term complications of head and neck irradiation that has a significant impact on the patient's daily living. Chronic RIX results in severe side effects, including difficulty swallowing, or dysphagia, oral discomfort, malnutrition, oral mucositis, changes in taste, increased oral infections and dental cavities.

#### *Our Gene Therapy Program—RIX*

Salivary glands are an attractive target organ for gene therapy treatments because they are self-contained, partially immune protected and easily accessible, allowing for non-invasive delivery of small vector doses.

We are developing AAV-AQP1 to treat RIX by increasing water conduction in the chronically damaged salivary glands by introducing a water conducting channel into the remaining epithelial cells of these damaged glands. Adequate water secretion by surviving epithelial cells has the potential to deliver the protective exocrine proteins produced by remaining gland cells into the mouth.

The key to our approach is that, unlike the water conducting acinar cells, the water impermeable duct cells of the glands appear to be resilient to IR exposure. As a consequence of this relative resilience to radiation treatment, salivary glands damaged by radiation treatment tend to contain mostly water impermeable ductal epithelial cells. To make these duct cells permeable to water, AAV-AQP1 introduces the gene for the human aquaporin water channel, or *hAQP1*. We have demonstrated that this has the potential to convey water permeability and causes ductal cells to generate an osmotic gradient, which causes them to secrete fluid into the lumen of the duct.

The proof of concept for this mechanism and its ability to increase the volume of saliva secreted by damaged salivary glands was observed in a Phase 1/2 clinical trial conducted by the U.S. National Institutes of Health, or NIH, in patients with chronic grade 2 or 3 RIX. The trial was designed as a short-term dose escalation trial of doses of AAV-AQP1 between  $4.8E7$  and  $5.8E9$  pu/gland using adenovirus as the vector to deliver the *hAQP1* to the remaining epithelial cells in the parotid gland of 11 patients suffering from chronic RIX. There were no reported severe adverse events among the patients treated, two out of three patients in each of the first three cohorts in this clinical trial were observed to have objective increases in saliva volume produced by the treated parotid gland, with increases in parotid flow ranging from 60% to 540%, and all but one of these patients showed a decrease in symptoms of dry mouth as measured by subjective visual analog scales, validated in other forms of xerostomia. The results of this study were published in *Proceedings of the National Academy of Sciences* in 2012.

We are currently conducting a Phase 1 dose escalation clinical trial in patients with grade 2 or 3 RIX who remain cancer free for at least five years after receiving radiation treatment. In this trial we are using AAV2 to deliver the *hAQP1* gene, as we believe AAV2 efficiently transfects the salivary gland cells and does not spread beyond the target cells. Up to 18 adult patients may be administered doses of AAV-AQP1 between  $3E9$  and  $6E11$  viral particles per gland in dose escalation cohorts of three patients each. The aim of the trial is to determine the safety of inserting *hAQP1* locally into the salivary glands of RIX patients, as well as to measure changes in salivary flow resulting from the introduction of this channel. We have completed dosing in the first cohort and begun dosing in the second cohort, having treated five patients. This clinical trial is being conducted in conjunction with the National Institute of Dental and Craniofacial Research at the NIH Dental Clinic.

We expect to initiate an additional clinical trial at Memorial Sloan Kettering Cancer Center in the second half of 2018.

The FDA granted orphan drug designation for AAV-AQP1 to treat symptoms of grade 2 and grade 3 late xerostomia from parotid gland hypofunction caused by radiotherapy for cancer of the oral cavity.

### *Sjogren's Syndrome*

The destruction of salivary tissue resulting in chronic xerostomia may also be caused by chronic autoimmune disease. Sjogren's syndrome is an autoimmune disease in which a patient's immune system may target the salivary glands. Chronic inflammation of the salivary glands results in long term damage and chronic xerostomia in many Sjogren's patients. Data from preclinical studies in animal models of Sjogren's syndrome and data from explants of minor salivary glands of Sjogren's patients suggest that Sjogren's syndrome may also be treatable with our AAV-AQP1 vector. Supported by data from our preclinical studies and our ongoing RIX clinical trials, we anticipate initiating a clinical trial of AAV-AQP1 for xerostomia caused by Sjogren's syndrome in 2019.

### **Neurodegenerative Diseases**

We also have research and preclinical programs targeting neurodegenerative diseases, with a research focus in ALS and Alzheimer's disease. In each of these diseases, we aim to target what we believe is a central factor in the underlying cell biology of the diseases, specifically RNA metabolism in ALS and endosomal trafficking dysfunction in Alzheimer's disease. Relying on our expertise in viral vector design, delivery, production and manufacturing, we are aiming to develop and optimize vectors to effectively treat both genetic and sporadic forms of these diseases.

### **ALS**

#### *Disease Background and Market Opportunity*

ALS is a devastating, progressive, neurodegenerative disease leading to the loss of motor neurons, which are the neurons that control the ability to move, speak, swallow and ultimately to breathe. The gradual paralysis in ALS invariably leads to death. While 10% of ALS cases are caused by inherited genetic mutations, most ALS occurs sporadically, with no known genetic cause. Mutations in over 20 genes have been identified that cause the inherited ALS cases. Characterization of these disease-causing genes have implicated several cellular pathways in the disease, with a prominent role emerging for genes involved in the cellular control of RNA. Many new regulatory roles are being discovered for RNA, particularly in neurons.

One gene linked to ALS is the transactive response DNA-binding protein 43, or *TDP-43*. The TDP-43 protein is one of a number of proteins that binds to cellular RNA and regulates its function and stability. When *TDP-43* does not function normally, RNA regulation in the neurons loses its tight control and the motor neurons die. While mutations in *TDP-43* account for only about 0.5% of ALS cases, aggregates of TDP-43 protein are observed in motor neurons of more than 95% of all ALS patients, including both inherited and sporadic, and TDP-43 aggregation is a central feature of diseased motor neurons in ALS patients. *TDP-43*, therefore, may be a critical therapeutic target for the treatment of both sporadic and inherited forms of ALS. TDP-43 aggregates are also seen in approximately 50% of patients with frontotemporal dementia, or FTD, suggesting a potentially similar underlying mechanism of this neurodegenerative disease.

#### *Our Gene Therapy Approach*

Genetic approaches using yeast as the primary model system have been used to identify ways of protecting motor neurons from death in ALS. A genetic screen was conducted to look for activated genes that rescue the toxicity of TDP-43 aggregation. A group of five genes that reduce TDP-43 toxicity, was identified including members of the nonsense mediated decay, or NMD, machinery, and two genes in particular: up frameshift protein 1, or *UPF1*, and up frameshift protein 2, or *UPF2*.

NMD is the quality control system regulating RNA processing and activity in all cells, and has additional and broader functions specifically in regulating RNA in neurons.

Over the past decade, increasing evidence suggests that motor neurons may be particularly vulnerable to defects in RNA regulation, which may be caused by a number of defects, including *TDP-43* aggregation. We believe that increasing the master quality control machinery for RNA processing, NMD, in motor neurons may improve the ability of motor neurons to survive in ALS.

We have designed a viral vector product candidate, AAV-UPF1, with the aim of increasing *UPF1* expression in the motor neurons of ALS patients. In preclinical studies, we observed that administration of AAV-UPF1 reduced motor neuron death thought to be driven by the toxic effects of several different genetic causes of ALS including, *TDP-43*, *FUS* and *C9orf72*. Improvements in ALS-like symptoms related to limb strength and mobility in rodent models of ALS have also been observed following administration of AAV-UPF1.

We believe that gene therapy using AAV-UPF1 may increase *UPF1* levels in cells affected by ALS, and we intend to deliver our viral vector product candidate to the central nervous system via intrathecal injection, or injection into the spinal canal. We are currently conducting IND enabling studies in animal models and have observed the preservation of neurons and a positive impact on functional endpoints in *Fus* and *TDP-43* neuronal cell cultures. Data is expected to become available on studies regarding modes of central nervous system delivery in non-human primates during 2018 and head-to-head non-human primates capsid study is set to launch during the second half of 2018. In the second half of 2018 we anticipate initiating manufacturing for our ALS program and engaging the FDA in pre-IND discussions, with the goal of filing an IND and initiating a clinical trial of AAV-UPF1 in ALS patients in 2019.

## **Alzheimer's Disease**

### *Disease Background and Market Opportunity*

With the world population aging, Alzheimer's disease has emerged as an extremely common and costly disease. While some treatments that have temporary effects on Alzheimer's disease symptoms are available, there is currently no approved treatment that halts the progression of the disease. Two biological pathways have been identified that are considered causes of Alzheimer's disease. They are identified as causative because mutations in genes that affect these pathways alone cause patients to develop the disease. The first causative pathway, identified in rare forms of early onset Alzheimer's disease, is the misprocessing of amyloid precursor protein, or APP, caused by genetic defects in *APP* itself and the APP processing proteins presenilin 1 and 2. The second causative pathway is related to the correct movement, or trafficking, of cellular protein which is controlled by a cell component called the endosome. Loss of function mutations in the endosomal protein sortilin-related receptor 1, or *SORL1*, have recently been shown to cause Alzheimer's disease.

The endosome is an organelle within the cell that is responsible for correctly directing protein trafficking to different sites within the cell as well as to the cell surface. In neurons, there is significant protein trafficking, particularly at dendrites or neuronal connections where the endosomal trafficking system regulates the movement of the cell signaling machinery that allows neurons to communicate with one another.

The molecular machine that drives endosomal protein trafficking is made up of a complex of proteins together called the retromer. The protein encoded by the Alzheimer's disease causing gene *SORL1* is a retromer component. *SORL1* and other components of the retromer complex are commonly deficient in Alzheimer's disease patients' brains. Defects in the endosomal trafficking pathway have also been implicated in other neurodegenerative diseases, including Parkinson's disease, ALS and frontotemporal dementia.

### *Our Gene Therapy Approach*

Our Alzheimer's disease program focuses on the endosomal trafficking pathway. In preclinical studies, we observed that increasing levels of key retromer proteins may reverse endosomal trafficking defects. We are identifying suitable retromer targets for gene augmentation in pre-symptomatic Alzheimer's patients.



There are several reasons why gene therapy is, in principle, well suited for Alzheimer's disease and other neurodegenerative diseases. The first relates to the pathophysiology, time course, and anatomical spread of these disorders. Neurodegenerative diseases generally begin locally in selectively vulnerable regions with "cell sickness" years before rampant cell death and wide-spread anatomical distribution. To be most effective, we believe interventions should be administered early and will benefit from local delivery. Even then, however, an intervention must maintain its efficacy for years because, unlike other cells in the body, neurons do not typically divide over the course of their life. We believe AAV-delivered gene therapy products may have a durable effect. In the best case scenario, one delivery successfully taken up by targeted neurons would be sufficient for years of efficacy.

An important component of our approach is the development and validation of surrogate markers of endosomal dysfunction and predictive markers of Alzheimer's disease. In particular, several well studied biomarkers linked to Alzheimer's disease, such as amyloid-beta and tau, have also been shown to be biomarkers of endosomal trafficking dysfunction in neurons. Such biomarkers could potentially be used to identify patients with Alzheimer's disease, as well as demonstrate potential product efficacy in the absence of Alzheimer's disease symptoms. By targeting endosomal trafficking dysregulation we aim to address the underlying cause of Alzheimer's disease as well as other neurodegenerative diseases, such as certain forms of Parkinson's disease.

### ***Our Gene Regulation Platform***

We are developing a potentially transformative technology designed to enable us to use small molecules to turn gene therapy product candidates on and off. The aim of this gene regulation platform is to transform gene therapy into a generalizable mechanism for the delivery of biologic drugs. The idea is that the gene encoding a particular biologic drug, for example epoetin alfa, or a therapeutic antibody, would be delivered to target cells in the body, but these genes would only be activated in the presence of a specific small molecule. The therapeutic protein would be manufactured by the body only in the presence of the small molecule so that intermittent production of the therapeutic protein would be achieved by dosing with the small molecule drug.

This temporal regulation of gene therapy products by exogenous small molecules has long been a goal of gene therapy researchers. The ability to regulate transgenes by introducing temporal control has the potential to transform the gene therapy landscape and the biologics industry as a whole. Our approach focuses on riboswitches to regulate gene expression rather than on the modulation of transcription factor activity, and this is the basis of our gene regulation platform.

Riboswitches are pieces of RNA that fold into alternative shapes depending on the binding of a specific small molecule to that RNA sequence. One RNA shape allows the gene containing the riboswitch to be active, while the alternative shape inactivates the gene. Riboswitches are used extensively by bacteria, but none have been identified in mammalian cells to date.

We designed a *de-novo* mammalian riboswitch that we have observed responds to small molecules and switch genes on and off in mammalian cells. Our riboswitch contains a stretch of RNA sequence, called an aptamer, that binds to a specific small molecule. The riboswitch is inserted into the therapeutic transgene cDNA. In the absence of the specific small molecule, the unbound riboswitch folds into the shape that drives the destruction of the entire RNA message and no therapeutic protein is produced in the absence of the small molecule. However, when the small molecule is present and binds to the riboswitch it adopts the alternative RNA shape, causing stable messages to be formed and the therapeutic protein to be produced.

One of the features of our mammalian riboswitch is its range of regulation. Using a small molecule we were able to switch the riboswitch containing gene on to levels greater than 1,000x higher than in the absence of the small molecule. We believe this technology is viable for a therapeutic product and is also the first instance of a proprietary system for screening randomized aptamers and small molecules within mammalian cells for functional interactions.

## **Our Manufacturing Capabilities**

We recently completed our cGMP manufacturing facility situated in London, United Kingdom. Supporting our global approach to clinical development and market supply, we designed the 29,000 square foot facility to meet multiple regulatory standards, including the Medicines and Health Products Regulatory Agency, or MHRA, in the UK, EMA and FDA standards. We recently had our final MHRA certification inspection.

We believe our facility can supply all of our current clinical and preclinical programs through regulatory approval and, should they be approved, provide sufficient capacity, for commercial production. Strategically, we believe our facility will minimize our dependence on third-party CMOs, which we believe provides a significant strategic, clinical and commercial advantage.

Our facility is flexible and scalable, with eleven independent air handling units, two cell culture suites and three separate viral vector production suites, which allows us to produce multiple product candidates in parallel, as well as sequentially at different scales. This allows us to accommodate up to three independent parallel manufacturing streams of viral products that are isolated within dedicated production areas.

Our manufacturing facility includes an integrated analytical department and in-house analytical tool kit that allows for in-house release of clinical and commercial manufactured products. Equipped with dedicated areas for microbiology, molecular biology, and cell-based analytics. Our analytical department can perform product related assays, allowing us to retain and gain expertise that is normally lost to third parties. The close integration allows for rapid turnaround and flexibility in scheduling of key assays, reducing lead times for product candidate releases. Further, our dedicated product fill and finish suite allows us to manufacture a full range of clinical and commercial products under one roof and in our control.

We have more than 40 highly trained multidisciplinary staff on our manufacturing team with backgrounds in manufacturing, managing and delivering gene therapy products.

We have identified and licensed a proprietary HEK293 cell line that is well characterized and that we have banked in 400 vials. The specific cell line, size of the bank, culture media, and cryopreservation agents have been selected to facilitate bridging between process development platforms and targets. Our HEK-293 cells lack the T antigen component and are suitable for both the current adherent culture platform and the bioreactor process. We believe the ability to use the same cell line throughout the product and process development lifecycle will allow us to use a bracketed approach to process validation and comparability, which we believe may reduce the time and costs related to their implementation.

## **Competition**

The biotechnology and pharmaceutical industries are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. This is true in the field of gene therapy generally, and in the treatments for our key disease areas. While we believe that the strength of our team, gene therapy expertise, scientific knowledge and intellectual property provide us with competitive advantages, we face competition from several sources, including large and small biopharmaceutical companies, academic research institutions, government agencies and public and private research institutions. Not only must we compete with other companies that are focused on gene therapy, but any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, clinical trials, regulatory approvals and product marketing than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, clinical programs. Mergers and acquisitions in the pharmaceutical and

biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

There are other organizations working to improve existing therapies or to develop new therapies for our initially selected disease indications. Depending on how successful these efforts are, it is possible they may increase the barriers to adoption and success for our product candidates, if approved. These efforts include two product candidates Applied Genetic Technologies Corporation, or AGTC, have in Phase 1/2 clinical trials to treat ACHM related to *CNGB3* and *CNGA3*, respectively, a product candidate in Phase 1/2 clinical trials by Nightstar Therapeutics plc and a program AGTC is running to treat XLRP, as well as Luxturna, which is marketed by Spark Therapeutics, Inc. and has been approved to treat *RPE65*-deficiency. We are not aware of any other gene therapy product candidates in clinical development targeting xerostomia. We are aware of other ALS gene therapies utilizing different treatment mechanisms to treat different genetically defined subsets of ALS patients.

We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. We expect any treatments that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

## **Intellectual Property**

Our success depends in large part upon our ability to secure and maintain proprietary protection for our technologies and products and to operate without infringing the proprietary rights of others. Our policy is to protect our proprietary position by, among other methods, filing or collaborating with our licensors to file U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also use other forms of protection, such as confidential information and trademark protection, particularly where we do not believe patent protection is appropriate or obtainable. Our patent portfolio consists of a combination of issued patents and pending patent applications that are owned or licensed from third parties.

As of March 1, 2018, we own, have an exclusive license or co-exclusive license under, or an exclusive option to license 27 United States and foreign issued patents and 93 patent applications, pending in the United States and internationally. For any individual patent, the term depends on the applicable law in the country in which the patent is granted. In most countries where we have filed patent applications or in-licensed patents and patent applications, patents have a term of 20 years from the application filing date or earliest claimed non-provisional priority date. In the United States, the patent term is 20 years but may be shortened if a patent is terminally disclaimed over another patent that expires earlier. The term of a U.S. patent may also be lengthened by a patent term adjustment, in order to address administrative delays by the United States Patent and Trademark Office in granting a patent. In the United States, the term of a patent that covers an FDA-approved drug or biologic may be eligible for patent term extension in order to restore the period of a patent term lost during the premarket FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the natural expiration of the patent. The patent term restoration period is generally equal to the regulatory review period for the approved product which period occurs after the date the patent issued, subject to certain exceptions. Only one patent may be extended for a regulatory review period for any product, and the application for the extension must be submitted prior to the expiration of the patent. In the future, we may decide to apply for restoration of patent term for one of our currently owned or licensed patents to extend its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

## **Company-Owned Intellectual Property**

We own six patent families relating to gene regulation platform technologies developed by us. The first patent family, includes 21 pending patent applications with claims directed to compositions of matter and

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methods of use in the United States, Europe, Australia, Canada, China, India, Japan, Brazil, Egypt, Indonesia, Israel, Republic of Korea, Malaysia, Mexico, New Zealand, Vietnam, African Regional IPO, Philippines, Singapore, South Africa and Eurasia. Patents issued from this family are expected to expire February 2, 2036, not including any patent term adjustments that may extend the patent term in certain jurisdictions. The other five families include five international applications relating to different gene regulations platform technologies with claims directed to compositions of matter and methods of use. We expect to convert each of these international applications to U.S. and international patent filings in due course. Patents issued from these five patent families are expected to expire in 2037 and 2038, not including any patent term adjustments that may extend the patent term in certain jurisdictions.

### **Licensed Intellectual Property**

Certain of our issued patents and pending patent applications are exclusively licensed to us from UCLB and Brandeis.

#### *UCLB*

The UCLB portfolio includes three licensed patent families relating to our *RPE65*, *CNGA3*, and *RPGR* gene therapy programs and one optioned patent family relating to our dry AMD gene therapy program with a combined 46 pending patent applications.

The first patent family, with claims directed to compositions of matter and methods of use relating to our *RPE65* program, and the AAV-*RPE65* product candidate includes 17 pending patent applications in the United States, Europe, Australia, Canada, China, India, Japan, Brazil, Egypt, Israel, Malaysia, Mexico, New Zealand, Nigeria, Philippines, Singapore, and Thailand. Patents issued from this family are expected to expire February 8, 2036, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

The second patent family, with claims directed to compositions of matter and methods of use relating to our achromatopsia program and the AAV-*CNGA3* product candidate, includes one pending patent application, which we expect to convert to an international application and subsequent U.S. and international patent filings in due course. Patents issued from this family are expected to expire in 2039, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

The third patent family, with claims directed to compositions of matter and methods of use relating to our retinitis pigmentosa program and the AAV-*RPGR* product candidate, includes five pending applications in the United States, Europe, Canada, China, and Japan. Patents issued from this family are expected to expire in July 2035, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

The fourth patent family which we have optioned, with claims directed to compositions of matter and methods of use relating to our dry AMD gene therapy program, includes 23 pending applications in the United States, Europe, Australia, Canada, China, India, Japan, Brazil, Egypt, Indonesia, Israel, Republic of Korea, Malaysia, Mexico, New Zealand, Nigeria, Vietnam, African Regional IPO, Philippines, Singapore, South Africa, Thailand and Eurasia. Patents issued from this family are expected to expire February 2036, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

#### *Brandeis*

The licensed Brandeis portfolio includes one patent family with claims directed to compositions of matter and methods of use relating to our ALS gene therapy program and the AAV-*UPF1* product candidate. This patent family includes an issued patent in Australia and pending patent applications in the United States, Europe, Canada and Hong Kong. Patents issued from this family are expected to expire October 8, 2033, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

## License Agreements

### *License Agreement between Athena and UCLB*

In February 2015, Athena entered into a license agreement with UCLB (the license agreement, together with all applicable amendments, is referred to as the First UCLB License Agreement, and together with all addendums, the First UCLB Agreement). In March 2016, all of Athena's rights, obligations, and liabilities under the First UCLB Agreement and all of its subsequent amendments, supplements, addendums and modifications were novated to us under a deed of novation. Pursuant to the First UCLB Agreement, UCLB granted Athena an exclusive, worldwide, and sublicensable license under certain intellectual property rights controlled by UCLB related to our *RPE65* and *CNGA3* and *CNGB3* gene therapy programs, including certain patent filings with claims directed to compositions of matter and methods of use relating to our *RPE65* program and the AAV-RPE65 product candidate, to develop and commercialize licensed products in the field of ocular gene therapy. We must use diligent efforts to develop and commercialize the licensed products.

In addition, under the terms of the First UCLB Agreement, we have an exclusive option to negotiate and enter into license addendums, or Athena Addendums, pursuant to which we would obtain royalty-bearing licenses under certain additional intellectual property rights, including certain patent filings relating to our dry AMD gene therapy program, on reasonable commercial terms. Such option expires on February 4, 2019.

Under the terms of the First UCLB Agreement, we issued a certain number of our ordinary shares to UCLB in accordance with a certain shareholder's agreement, or the Athena Shareholders' Agreement. We are also required to pay UCLB sales milestone payments of up to a total of £39.75 million in the aggregate and an annual management fee of £50,000 until certain royalty payments have been paid.

Commencing on the first commercial sale of licensed products, we must make low single-digit percentage royalty payments to UCLB on net sales of such products. Our royalty obligations under the agreement continue on a licensed product-by-licensed product and country-by-country basis until the earlier to occur of (a) the expiration of the last valid claim of a patent claiming such licensed product in such country, or (b) the 10th anniversary of the first commercial sale of such licensed product in such country. In addition, we must pay UCLB mid-twenty percentages of certain sublicensing revenues.

Unless terminated earlier, the First UCLB License Agreement will remain in effect until the expiration or termination of the last Athena Addendum. The First UCLB License Agreement may be terminated: (a) by either party in the event of the other party's material breach that remains uncured for 30 days (or for 14 days in the case of breaches related to payment obligations), (b) by UCLB in the event of our material breach of the Athena Shareholders' Agreement that remains uncured for 30 days, (c) by either party for the other party's insolvency, (d) immediately by UCLB if we challenge the validity or ownership of UCLB's patents, (e) immediately by UCLB if we are in persistent breach of the First UCLB License Agreement and the parties fail to agree upon a mechanism to remedy such persistent breach (or we do not comply with such agreed upon mechanism), (f) immediately by UCLB if we are in material breach of the First UCLB License Agreement more than twice in any 24-month period, even if such breaches have been remedied, or (g) immediately by UCLB if we undergo certain change of control events or if we enter into a sublicense with certain prohibited persons which may adversely affect UCL's and/or UCLB's reputation.

Unless terminated earlier, each Athena Addendum will remain in effect on a country-by-country basis until the expiration of the last payment obligation under the First UCLB Agreement. Each Athena Addendum may be terminated: (a) by either party in the event of the other party's material breach that remains uncured for 30 days (or for 14 days in the case of breaches related to payment obligations), (b) by UCLB if we fail to achieve any of the milestone events in the applicable Athena Addendum within six months after the applicable milestone deadline, (c) immediately by UCLB if we challenge the validity or ownership of UCLB's patents, (d) by UCLB if we fail to provide an updated development plan for the relevant Athena Addendum within six months of the

effective date of such Athena Addendum, (e) immediately by UCLB if we are in persistent breach of the relevant Athena Addendum and the parties fail to agree upon a mechanism to remedy such persistent breach (or we do not comply with such agreed upon mechanism), or (f) immediately by UCLB if we are in material breach of the relevant Athena Addendum more than twice in any 24-month period, even if such breaches have been remedied. Each Athena Addendum may also be terminated, or the exclusive licenses granted under the relevant Athena Addendum may be converted to a non-exclusive license, by UCLB upon three-months' notice if we, based on an independent expert determination, fail to use diligent efforts to achieve certain milestone events or to develop and commercially exploit licensed products and do not cure such failure within a certain cure period.

#### ***License Agreements with UCLB***

##### *July 2017 Agreement with UCLB*

In July 2017, we entered into a license agreement with UCLB, or the Second UCLB Agreement. Pursuant to the Second UCLB Agreement, UCLB granted us an exclusive, worldwide, and sublicensable license under certain intellectual property rights, including certain patent filings, controlled by UCLB with claims directed to compositions of matter and methods of use relating to our retinitis pigmentosa gene therapy program and the AAV-RPGR product candidate to develop and commercialize licensed products in the field of ocular gene therapy. We must use diligent efforts to develop and commercialize the licensed products. Under the terms of the Second UCLB Agreement, we paid an initial upfront payment of \$17,888. We are also required to pay UCLB sales milestone payments of up to a total of £39.75 million in the aggregate and an annual management fee of £50,000 until certain royalty payments have been paid.

Commencing on the first commercial sale of licensed products, we must make low single-digit percentage royalty payments to UCLB on net sales of such products. Our royalty obligations under the agreement continue on a licensed product-by-licensed product and country-by-country basis until the latest to occur of the expiration of the last valid claim of a patent claiming such licensed product in such country, the expiration of regulatory exclusivity for such licensed product in such country, or the 10th anniversary of first commercial sale of such licensed product in such country. The Second UCLB Agreement will remain in effect on a country-by-country basis until the expiration of the last payment obligation in such country. The Second UCLB Agreement may be terminated: (a) by either party in the event of the other party's material breach that remains uncured for 30 days, (b) by either party for the other party's insolvency, or (c) immediately by UCLB if we are in persistent breach of the Second UCLB Agreement and the parties fail to agree upon, within a reasonable amount of time, a mechanism to remedy such persistent breach (or we do not comply with such agreed upon mechanism), or (d) immediately by UCLB if we undergo certain change of control events or if we enter into a sublicense with certain prohibited persons which may adversely affect UCL's and/or UCLB's reputation. The Second UCLB Agreement may also be terminated or converted to a non-exclusive license by UCLB upon three months' notice if we, based on an independent expert determination, fail to use diligent efforts to develop and commercially exploit licensed products and do not cure such failure within a certain cure period.

##### *March 2018 Agreement with UCLB*

In March 2018, we, together with MeiraGTx UK II, entered into a license agreement with UCLB, or the Third UCLB Agreement. As of March 2018, the Third UCLB Agreement supersedes the Athena Agreement regarding the CNGA3 program. Pursuant to the Third UCLB Agreement, UCLB granted us an exclusive, worldwide, and sublicensable license under certain intellectual property rights controlled by UCLB, including a certain patent filing with claims directed to compositions of matter and methods of use relating to our achromatopsia gene therapy program and the AAV-CNGA3 product candidate to develop and commercialize licensed products in the field of ocular gene therapy. We must use diligent efforts to develop and commercialize the licensed products.

Under the terms of the Third UCLB Agreement, we paid an initial upfront payment of £6,994, and issued certain number of shares with equivalent cash value of £100,000 to UCLB. We are also required to pay

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UCLB sales milestone payments of up to a total of £39.75 million in the aggregate and an annual management fee of £50,000 until certain royalty payments have been paid.

Commencing on the first commercial sale of licensed products, we must make low single-digit percentage royalty payments to UCLB on net sales of such products. Our royalty obligations under the agreement continue on a licensed product-by-licensed product and country-by-country basis until the latest to occur of the expiration of the last valid claim of a patent claiming such licensed product in such country, the expiration of any regulatory exclusivity for all licensed products in such country, or the tenth anniversary of first commercial sale of such licensed product in such country.

The Third UCLB Agreement will remain in effect on a country-by-country basis until the expiration of the last payment obligation in such country. The Third UCLB Agreement may be terminated: (a) by either party in the event of the other party's material breach that remains uncured for 30 days, (b) by either party for the other party's insolvency, (c) immediately by UCLB if we are in persistent breach of the Third UCLB Agreement and the parties fail to agree upon a mechanism to remedy such persistent breach (or we do not comply with such agreed upon mechanism), (d) immediately by UCLB if we fail to comply with certain obligations relating to the issuance of shares to UCLB under the Third UCLB Agreement, or (e) immediately by UCLB if we undergo certain change of control events or if we enter into a sublicense with certain prohibited persons, which may adversely affect UCLB's and/or UCLB's reputation. The Third UCLB Agreement may also be terminated or converted to a non-exclusive license by UCLB upon three months' notice if we, based on an independent expert determination, fail to use diligent efforts to develop and commercially exploit licensed products and do not cure such failure within a certain cure period.

### *License Agreement between Bri-Alzan Inc. and Brandeis*

In May 2013, BRI-Alzan Inc., or BRI-Alzan, entered into a license agreement with Brandeis, or the Brandeis Agreement. In 2015, we merged with BRI-Alzan, and the Brandeis Agreement was assigned to us as a result of such merger. Pursuant to the Brandeis Agreement, Brandeis granted us an exclusive, worldwide license under certain patent rights with claims directed to compositions of matter and methods of use relating to our ALS gene therapy program and the AAV-UPF1 product candidate to develop and commercialize licensed products.

We must use commercially reasonable efforts to develop and commercialize licensed products. We also acquired non-exclusive, worldwide licenses to certain know-how controlled by Brandeis' to exploit licensed products. We are required to pay Brandeis developmental and regulatory milestone payments of up to a total of \$1.0 million in the aggregate. We are also required to pay Brandeis annual license maintenance fees ranging from \$15,000 to \$100,000 depending on the development stage of the licensed product. Commencing on the first commercial sale of licensed products, we must make low single-digit percentage royalty payments to Brandeis on net sales of such products. In addition, we must pay Brandeis mid-teen percentages of sublicensing revenues.

The Brandeis Agreement will remain in effect on a country-by-country basis until the earlier of: (a) 1 year after the date that we, our affiliates or sublicensees last sell any licensed product in such country or (b) until the expiration of the last-to-expire of the licensed patent rights in such country. The Brandeis Agreement may be terminated by Brandeis for our insolvency or for our material breach that remains uncured for 60 days (or for 30 days in the case of breaches related to payment obligations). Such material breach may be cured only once in any 12-month period. Brandeis may also terminate any license granted under the Brandeis Agreement if we fail to timely achieve certain regulatory milestone events.

### **Trade Secrets**

We also rely on trade secrets, technical know-how and continuing innovation to develop and maintain our competitive advantage. Our policy requires inventors who are identified on any company-owned patent applications to assign rights to us. We also rely on confidentiality agreements with our employees, consultants

and other advisors to protect our proprietary information. Our policy is to require third parties that receive material confidential information to enter into confidentiality agreements with us.

### **Trademarks**

Our trademark MeiraGTx has been registered in the European Union and a U.S. application is pending.

### **Government Regulation and Product Approval**

Governmental authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing, post-approval monitoring and reporting and export and import of products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, are extensive and require the expenditure of substantial time and financial resources.

### **FDA Approval Process**

We expect our future product candidates to be regulated as biologics. Biological products, including gene therapy products, are subject to extensive regulation by the FDA under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and other federal, state, local and foreign statutes and regulations. Both the FDCA and the PHSA and their corresponding regulations govern, among other things, the research, development, safety, testing, packaging, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of biological products. Before clinical testing of biological products in the United States may begin, we must submit an investigational new drug application, or IND, to the FDA, which reviews the clinical protocol, and the IND must become effective before clinical trials may begin. In some instances, we must also submit our protocols to the National Institutes of Health, or NIH, through its Recombinant DNA Advisory Committee, or RAC, for review before initiating clinical testing of gene therapy products.

Gene therapy products must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agencies before they may be legally marketed in foreign countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. The CBER works closely with the NIH and its RAC, which makes recommendations to the NIH on gene therapy issues and engages in a public discussion of scientific, safety, ethical and societal issues related to proposed and ongoing gene therapy protocols. The FDA has published guidance documents with respect to the development and submission of gene therapy protocols. The FDA also has published guidance documents related to, among other things, gene therapy products in general, their preclinical assessment, observing subjects involved in gene therapy clinical trials for delayed adverse events, potency testing, and chemistry, manufacturing and control information in gene therapy INDs.

To date, the FDA has approved three human gene therapy products for sale, including Kite Pharma's Yescarta, Novartis' Kymriah and Spark's Luxturna, and has provided general guidance regarding the development of gene therapy products. For example, the FDA has established the Office of Tissue and Advanced Therapies within CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee, to advise CBER on its reviews. In addition, the FDA has issued a growing body of clinical guidelines, chemical, manufacturing and control, or CMC, guidelines and other guidelines, all of which are intended to facilitate industry's development of gene therapy products.



Ethical, social and legal concerns about gene-editing technology, gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating biotechnology. More restrictive regulations or claims that our products are unsafe or pose a hazard could prevent us from commercializing any product candidates. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

*U.S. Biological Products Development Process*

The FDA determined that more than minimally manipulated products must be approved by the FDA through the Biologics License Application, or BLA, process before they may be legally marketed in the United States. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- completion of extensive nonclinical, sometimes referred to as preclinical laboratory tests, and preclinical studies and applicable requirements for the humane use of laboratory animals and formulation studies in accordance with applicable regulations, including good laboratory practices, or GLPs;
- submission to the FDA of an IND application, which must become effective before clinical trials may begin;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;
- submission to the FDA of a BLA for marketing approval that includes substantive evidence of safety, purity, potency and efficacy from results of nonclinical testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with cGMP to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical study sites that generated the data in support of the BLA; and
- FDA review and approval, or licensure, of the BLA.

Before testing any biological product candidate, including a gene therapy product, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLPs. The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing and controls, information about product chemistry, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some

preclinical testing, such as reproductive toxicity tests and carcinogenicity in animals, may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, after which human clinical trials may begin unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. With gene therapy protocols, if the FDA allows the IND to proceed, but a RAC decides that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trials. In addition to the IND submission process, sponsors of certain clinical trials of cells containing recombinant or synthetic nucleic acid molecules, including human gene transfer studies, must comply with the NIH's Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. The NIH Guidelines set forth the principles and requirements for NIH and institutional oversight of research with recombinant or synthetic nucleic acid molecules, including the standards for investigators and institutions to follow to ensure the safe handling and containment of such molecules. In April 2016, modifications to the NIH Guidelines went into effect, pursuant to which only a subset of human gene transfer protocols are subject to review by the RAC. Specifically, under the modified NIH Guidelines, RAC review of the protocol will be required only in exceptional cases where an oversight body such as an Institutional Biosafety Committee, or IBC, which provides local review and oversight of research utilizing recombinant or synthetic nucleic acid molecules, or an IRB determines that the protocol would significantly benefit from RAC review, and the protocol (a) uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience and thus presents an unknown risk, and/or (b) relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value, and/or (c) involves a proposed vector, gene construct, or method of delivery associated with possible toxicities that are not widely known and that may render it difficult for oversight bodies to evaluate the protocol rigorously. The RAC review proceedings are public, and reports are posted publicly to the website for the NIH's Office of Biotechnology Activities. Although compliance with the NIH Guidelines is mandatory for research conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Independent of RAC review, the NIH Guidelines also require all human gene transfer protocols subject to the NIH Guidelines to be registered with NIH, with limited exemptions. A study subject to the NIH Guidelines may not begin until the IBC approves the protocol, and the IBC cannot approve the protocol until confirmation from the NIH that such registration is complete. In the event that RAC review is warranted, the protocol registration process cannot be completed until RAC review has taken place.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, the efficacy measurements to be evaluated and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Clinical trials also must be reviewed by an IBC, a local institutional committee that reviews and oversees basic

and clinical research conducted at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biological product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2. The biological product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

In most cases, the FDA requires two adequate and well controlled Phase 3 clinical trials to demonstrate the safety and efficacy of a biological product. In rare instances, a single Phase 3 trial, together with other confirmatory evidence may be sufficient to support a BLA submission. Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by ten years of annual queries, either in person or by questionnaire.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other trials, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend or permanently discontinue a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk or the clinical trial is not being conducted in accordance with FDA regulations. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product candidate has been associated with unexpected serious harm to patients. The FDA and the IRB may also halt, terminate or impose other conditions if either believes the patients are subject to unacceptable risk.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov). Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the

results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

Human gene therapy products based on gene-editing technology are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the study period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of human gene therapy products, or that the data generated in these trials will be acceptable to the FDA to support marketing approval. The NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene transfer trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events in these trials.

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the physical characteristics of the biological product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

#### *U.S. Review and Approval Processes*

After the completion of clinical trials of a biological product candidate, FDA approval of a BLA must be obtained before commercial marketing and distribution of the biological product. The BLA must include results of product development, laboratory and animal trials, human trials, information on the manufacture, pharmacology, chemistry and controls of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective.

The Food and Drug Administration Safety and Innovation Act, or FDASIA, requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include, among other things, an outline of the pediatric study or studies that the sponsor plans to conduct, including to the extent practicable study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information, along with any other information specified in FDA regulations. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

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Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual program fee for products. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first human drug application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. Under PDUFA, the FDA has agreed to certain performance goals to complete the review of BLAs. The FDA may give a priority review designation to biological products that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the current PDUFA agreement, these six and ten month review periods are measured from the “filing” date rather than the receipt date for original BLAs, which typically adds approximately two months to the timeline for review and decision from the date of submission.

The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP requirements to assure and preserve the product’s identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product candidate. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. To assure cGMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. If, or when, those deficiencies have been addressed to the FDA’s satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. Under the current PDUFA guidelines, the FDA has committed to reviewing such resubmissions in two or six months of receipt depending on the type of information included.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with REMS, to ensure the benefits of the product outweigh its potential risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. The requirement for a REMS can materially affect the potential market and profitability of the product.

Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. Changes to some of the conditions established in an approved BLA, including changes in indications, product labeling, manufacturing processes or facilities, require submission and FDA approval of a new BLA or BLA supplement before the change can be implemented. A BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing BLA supplements as it does in reviewing BLAs. The FDA may require one or more Phase 4 post-market studies or surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Additionally, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs. For example, in December 2016, the 21st Century Cures Act was signed into law. This act is intended, among other things, to modernize the regulation of drugs and biologics and to spur innovation, and contains provisions specific to the development of cell therapies.

One of the performance goals agreed to by the FDA under the PDUFA is to review 90% of standard BLAs in ten months from the filing date and 90% of priority BLAs in six months from the filing date, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

### *Orphan Drug Designation*

The FDA may grant Orphan drug designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the drug or biologic for this type of disease or condition will be recovered from its sales in the United States. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the United States, Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and BLA user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application, including a full BLA, to market the same drug or biologic for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approved orphan-designated

product. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

#### *Expedited Development and Review Programs*

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new biological products that meet certain criteria. Specifically, new biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new biologic may request that the FDA designate the biologic as a Fast Track product at any time during the clinical development of the product. The FDA must determine if the biologic product candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval, which means that they may be approved on the basis of adequate and well controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a biological product subject to accelerated approval perform adequate and well-controlled post-marketing Phase 4 clinical trials. Failure to conduct required post-approval trials, or to confirm a clinical benefit during post-marketing trials, will allow the FDA to withdraw the approved biologic product from the market on an expedited basis. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

In addition, under the provisions of FDASIA, enacted in 2012, the FDA established a Breakthrough Therapy Designation which is intended to expedite the development and review of products that treat serious or life-threatening diseases or conditions. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and

preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the features of Fast Track designation, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy Designation is a distinct status from both accelerated approval and priority review, but these can also be granted to the same product candidate if the relevant criteria are met. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. All requests for breakthrough therapy designation will be reviewed within 60 days of receipt, and FDA will either grant or deny the request.

Furthermore, as part of its implementation of the 21st Century Cures Act, the FDA established the Regenerative Medicine Advanced Therapy, or RMAT, designation, to facilitate an efficient development program for, and expedite review of, certain drugs and biological products. A biological product is eligible for RMAT designation if it qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions, and is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and for which preliminary clinical evidence indicates that the biological product has the potential to address unmet medical needs for such a disease or condition. Like breakthrough therapy designation, RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. RMAT-designated products that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the submission of clinical evidence, clinical trials, patient registries, or other sources of real world evidence (such as electronic health records); through the collection of larger confirmatory data sets; or via post-approval monitoring of all patients treated with such therapy prior to approval of the therapy.

Fast Track designation, priority review, accelerated approval, breakthrough therapy designation and RMAT designation do not change the standards for approval but may expedite the development or approval process. Even if we receive one of these designations for our product candidates, the FDA may later decide that our product candidates no longer meets the conditions for qualification. In addition, receiving these designations may not provide us with a material commercial advantage.

### *Post-Approval Requirements*

Maintaining substantial compliance with applicable federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP requirements. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products, include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements.

After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may



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perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

To help reduce the increased risk of the introduction of adventitious agents, the PHS Act emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHS Act also provides authority to the FDA to immediately suspend biologics licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases within the United States.

The FDA may require one or more Phase 4 post-market trials or surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies. We also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

### *U.S. Patent Term Restoration and Marketing Exclusivity*

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under Hatch-Waxman Act. The Hatch-Waxman Act permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally equal to the regulatory review period for the approved product which period occurs after the date the patent issued, subject to certain exceptions. Only one patent may be extended for a regulatory review period for any product, and the application for the extension must be submitted prior to the

expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may intend to apply for restoration of patent term for one of our currently owned or licensed patents to extend its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

For patents that might expire during the BLA review phase, the patent owner may request an interim patent term extension. If eligible, an interim patent term extension may be granted for a period of not more than one year. The patent owner may apply for not more than four subsequent interim extensions. Any interim extension granted will not be longer than the maximum period of extension allowed post-approval.

### *Biosimilars and Exclusivity*

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, only a handful of biosimilars have been licensed under the BPCIA, and numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and meaning of the BPCIA remains subject to significant uncertainty.

### *Other Healthcare Laws and Compliance Requirements*

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws

include, without limitation: the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under any federal healthcare program; federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to the federal government, including federal healthcare programs, that are false or fraudulent; the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes which prohibit, among other things, executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters; HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, which imposes certain requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information; the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to the federal government, information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and state and foreign law equivalents of each of the above federal laws, which, in some cases, differ from each other in significant ways, and may not have the same effect, thus complicating compliance efforts. If their operations are found to be in violation of any of such laws or any other governmental regulations that apply, they may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of operations, exclusion from participation in federal and state healthcare programs and individual imprisonment.

#### *Coverage and Reimbursement*

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

#### *Healthcare Reform*

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly

affected by federal and state legislative initiatives, including those designed to limit the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded health care programs, and increased governmental control of drug pricing.

In March 2010, the ACA was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States, and significantly affected the pharmaceutical industry. The ACA contains a number of provisions of particular import to the pharmaceutical and biotechnology industries, including, but not limited to, those governing enrollment in federal healthcare programs, a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Most recently, the Tax Cuts and Jobs Act of 2017 was enacted, which, among other things, removes penalties for not complying with ACA's individual mandate to carry health insurance. There is still uncertainty with respect to the impact President Trump's administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

#### *U.S. Foreign Corrupt Practices Act*

The U.S. Foreign Corrupt Practices Act of 1977, or FCPA, prohibits U.S. corporations and individuals from engaging in certain activities to obtain or retain business or secure any improper advantage, or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any employee or official of a foreign government or public international organization, or political party, political party official, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. The scope of the FCPA also includes employees and officials of state-owned or controlled enterprises, which may include healthcare professionals in many countries. Equivalent laws have been adopted in other foreign countries that impose similar obligations.

#### ***Government Regulation Outside of the United States***

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our

products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application, or CTA, much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

#### *Clinical Trials*

Clinical trials of medicinal products in the European Union must be conducted in accordance with European Union and national regulations and the International Conference on Harmonization, or ICH, guidelines on GCPs. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products. If the sponsor of the clinical trial is not established within the European Union, it must appoint an entity within the European Union to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

Prior to commencing a clinical trial, the sponsor must obtain a clinical trial authorization from the competent authority, and a positive opinion from an independent ethics committee. The application for a clinical trial authorization must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. Currently, clinical trial authorization applications must be submitted to the competent authority in each EU Member State in which the trial will be conducted. Under the new Regulation on Clinical Trials, which is currently expected to take effect in 2019, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only a limited involvement. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be notified to or approved by the relevant competent authorities and ethics committees. Medicines used in clinical trials must be manufactured in accordance with cGMP. Other national and European Union-wide regulatory requirements also apply.

During the development of a medicinal product, the EMA and national medicines regulators within the European Union provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Scientific Advice Working Party of the Committee for Medicinal Products for Human Use, or CHMP. A fee is incurred with each scientific advice procedure. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical trials, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application of the product concerned.

#### *Marketing Authorizations*

To obtain regulatory approval of an investigational biological product under EU regulatory systems, we must submit a marketing authorization application. The application used to file the BLA in the United States is

similar to that required in the European Union, with the exception of, among other things, country-specific document requirements. The process for doing this depends, among other things, on the nature of the medicinal product.

The centralized procedure results in a single marketing authorization, or MA, granted by the European Commission that is valid across the EEA (i.e., the European Union as well as Iceland, Liechtenstein and Norway). The centralized procedure is compulsory for human drugs that are: (i) derived from biotechnology processes, such as genetic engineering, (ii) contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions and viral diseases, (iii) officially designated orphan medicines and (iv) advanced-therapy medicines, such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure may at the request of the applicant also be used in certain other cases. Therefore, the centralized procedure would be mandatory for the products we are developing.

The Committee for Advanced Therapies, or CAT, is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CAT is primarily responsible for the scientific evaluation of ATMPs and prepares a draft opinion on the quality, safety and efficacy of each ATMP for which a marketing authorization application is submitted. The CAT's opinion is then taken into account by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a marketing authorization application; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs. Although these guidelines are not legally binding, we believe that our compliance with them is likely necessary to gain and maintain approval for any of our product candidates.

Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days. This excludes so-called clock stops, during which additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. At the end of the review period, the CHMP provides an opinion to the European Commission. If this is opinion favorable, the Commission may then adopt a decision to grant an MA. In exceptional cases, the CHMP might perform an accelerated review of an MAA in no more than 150 days (not including clock stops). This is usually when the product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation.

The European Commission may grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The European Commission may also grant a so-called “marketing authorization under exceptional circumstances”. Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radio-pharmaceutical, by an authorized person; and

The package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a “normal” marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal. A marketing authorization under exceptional circumstances should not be granted when a conditional marketing authorization is more appropriate.

The European Union medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain EU Member States may prohibit or restrict us from commercializing our products, even if they have been granted an MA.

### *Data and Marketing Exclusivity*

The European Union also provides opportunities for market exclusivity. Marketing authorization applications for generic medicinal products do not need to include the results of preclinical and clinical trials, but instead can refer to the data included in the marketing authorization of a reference product for which regulatory data exclusivity has expired. In the European Union, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. The two-year period may be extended to three years if during the first eight years a new therapeutic indication with significant clinical benefit over existing therapies is approved. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator’s data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator’s data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the EU regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

There is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the European Union. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

### *Orphan Medicinal Products*

Products receiving orphan designation in the European Union can receive ten years of market exclusivity. During the ten year market exclusivity period, the EMA cannot accept another application for a marketing authorization, or grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indication, in respect of a similar medicinal product. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an “orphan medicinal product” in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers. The application for orphan drug designation must be submitted before the MAA. The applicant will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, an MA may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply enough orphan medicinal product.

### *Pediatric Investigation Plan*

In the EMA, MAAs for new medicinal products not authorized have to include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA’s Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which an MA is being sought. The PDCO can grant a deferral of the



obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU Member States and trial results are included in the product information, even when negative, the product is eligible for a six-months supplementary protection certificate extension.

### *Post-Approval Controls*

The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the marketing authorization. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions.

All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

### *Pricing and Reimbursement*

Governments influence the price of medicinal products in the European Union through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other EU Member States allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription medicines, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

### *PRIME Scheme*

In July 2016 the EMA launched PRIME scheme. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is however not guaranteed. The benefits of a PRIME designation includes the appointment of a rapporteur from the CHMP before submission of an MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

*UK Specials Regulation*

The UK's Human Medicines Regulations 2012 allow for the manufacture and supply of medicinal products not authorized for marketing to patients with special needs at the request of the healthcare professional responsible for the patient's care (these products are referred to as "specials"). A special may only be supplied in: (i) response to an unsolicited order from a healthcare professional responsible for the care of the patient, (ii) the product is manufactured and assembled in accordance with the specifications of that healthcare professional to fulfil the special needs of the individual patient which cannot be met by products already authorized for marketing, and (iii) the product is manufactured under a specials license granted by the UK's MHRA.

**Employees**

As of March 31, 2018, we had 59 employees, including 11 employees with M.D. or Ph.D. degrees. Of these full-time employees, 45 are engaged in research and development activities. None of our employees is subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relationship with our employees to be good.

**Facilities**

Our principal office is located at 430 East 29th Street, 10th Floor, New York, NY 10016, USA, where we lease 5,887 square feet of office space. We lease this office space under a lease that terminates on December 31, 2021.

We also lease the ground rights where our 29,000 square foot manufacturing facility is located, at 92 Britannia Walk, London N1 7NQ, United Kingdom. This lease terminates February 2, 2021 and we have the option to extend until February 2, 2026.

**Legal Proceedings**

We are not subject to any material legal proceedings.

## MANAGEMENT

### Executive Officers and Directors

The following table sets forth certain information of each executive officer and non-employee director of MeiraGTx Limited, including their ages as of May 14, 2018.

<u>Name</u>	<u>Age</u>	<u>Position</u>
<b>Executive Officers</b>		
Alexandria Forbes, Ph.D.	53	President and Chief Executive Officer and Director
Richard Giroux	45	Chief Operating Officer
Stuart Naylor, Ph.D.	54	Chief Development Officer and Director
<b>Non-employee Directors</b>		
Keith R. Harris, Ph.D.	65	Chairman of the Board
Ellen Hukkelhoven, Ph.D.	31	Director
Arnold J. Levine, Ph.D.	78	Director
Joel S. Marcus	70	Director
Neil Mendoza	58	Director
Gregory S. Moss	34	Director
Thomas E. Shenk, Ph.D.	71	Director

(1) Member of the audit committee.

(2) Member of the compensation committee.

(3) Member of the nominating and corporate governance committee.

### Executive Officers

*Alexandria Forbes, Ph.D.* has served as our President, Chief Executive Officer and member of our board of directors since March 2015. Prior to joining MeiraGTx, Dr. Forbes served as Senior Vice President of Commercial Operations at Kadmon Holdings, Inc., a biopharmaceutical company, from September 2013 to April 2015, and currently serves as a member of its board of directors. A subsidiary of Kadmon Holdings, Inc. is a holder of more than 5% of our outstanding shares. Prior to Kadmon Holdings, Inc., Dr. Forbes spent eleven years as a healthcare investor at Sivik Global Healthcare (formerly Argus Partners), a healthcare hedge fund, from August 2001 to November 2008, and at Meadowvale Asset Management, a healthcare hedge fund, from January 2010 to June 2012. Before entering the hedge fund industry, Dr. Forbes was a Human Frontiers/Howard Hughes postdoctoral fellow at the Skirball Institute of Biomolecular Medicine at NYU Langone Medical Center from March 1997 to September 2000. Prior to this, Dr. Forbes was a research fellow at Duke University, and also at the Carnegie Institute at Johns Hopkins University. Dr. Forbes received an M.A. in Natural Sciences from Cambridge University and a Ph.D. in Molecular Genetics from Oxford University. Our board of directors believes Dr. Forbes' extensive academic and clinical experience, as well as her knowledge of the industry, qualifies her to serve on our board of directors.

*Richard Giroux* has served as our Chief Operating Officer since March 2015. Mr. Giroux joined MeiraGTx from Sarissa Capital Management LP, an activist healthcare hedge fund, where he was a partner from March 2014 to March 2015. Prior to Sarissa Capital Management LP, Mr. Giroux was a founding partner and healthcare portfolio manager of Meadowvale Partners, a multi-strategy hedge fund, from January 2010 until June 2012. Prior to Meadowvale Partners, he was a partner at Sivik Global Healthcare (formerly Argus Partners), a healthcare hedge fund, from August 2001 to November 2008. Prior to that, he worked at investment banks Salomon Smith Barney and Goldman Sachs. Mr. Giroux received a B.A. in Economics from Yale University.

*Stuart Naylor, Ph.D.* has served as our Chief Development Officer and a member of our board of directors since April 2015. From April 2015 to April 2016, Dr. Naylor was Chief Executive Officer of Athena

Vision Limited, a biotechnology company. From June 2013 to April 2015, Dr. Naylor served as managing director of Coltivare Ltd., a healthcare consulting company. From 2008 to 2013, Dr. Naylor was Executive Director and Chief Scientific Officer of Oxford BioMedica plc, a gene therapy company. Prior to joining Oxford BioMedica plc, Dr. Naylor focused on translational cancer research at the Institute of Cancer Research in London. Dr. Naylor has a B.S.C. in microbiology and virology from the University of Warwick, an M.S. in Immunology from Kings College London, and a Ph.D. from the Imperial Cancer Research Fund laboratory studying ovarian cancer and cytokine biology. Our board of directors believes Dr. Naylor's extensive academic and clinical experience, as well as his knowledge of the industry, qualifies him to serve on our board of directors.

#### **Non-employee Directors**

*Keith Harris, Ph.D.* has served as a member of our board of directors since June 2015 and served as chairman of our board of directors since February 2018. Dr. Harris is a London-based investment banker and financier with a 25-year career as a senior corporate finance and takeover advisor. Since 1999, Dr. Harris has been the chairman of Keith Harris & Associates, a sports consulting firm. Dr. Harris previously served as Chief Executive Officer of HSBC Investment Bank from 1994 to 1999 and Seymour Pierce Holdings Limited, a subsidiary of which, Seymour Pierce Limited, was acquired in a pre-paid administration under U.K. law in 2013. Dr. Harris received a B.A. in business and economics from the University of Bradford and a Ph.D. in Economics from the University of Surrey. Our board of directors believes that Dr. Harris' financial knowledge and experience qualifies him to serve as a member of our board of directors.

*Ellen Hukkelhoven, Ph.D.* has served as a member of our board of directors since October 2017. Dr. Hukkelhoven currently serves as a Senior Analyst at Perceptive Advisors, a leading healthcare investment firm. Prior to joining Perceptive Advisors in 2013, Dr. Hukkelhoven received an A.B. in molecular biology from Princeton University and a Ph.D. in cancer biology from Memorial Sloan Kettering Cancer Center. Our board of directors believes that Dr. Hukkelhoven's academic and biotechnology investing experience qualifies her to serve as a member of our board of directors.

*Arnold J. Levine, Ph.D.* has served as a member of our board of directors since February 2016. Dr. Levine currently serves as a professor emeritus at the Institute for Advanced Study at Princeton University. Dr. Levine was a director of Imclone Systems Incorporated from 2000 to 2003. He was a professor in the Department of Molecular Biology at Princeton University from 1984 until 1996, where he was named the Harry C. Wiess Professor in Life Sciences and was the chairman of the department. Dr. Levine received a B.A. from Harpur College, State University of New York at Binghamton and a Ph.D. in microbiology from the University of Pennsylvania. Our board of directors believes Dr. Levine's expertise and experience serving as a director in the pharmaceutical sector and his academic background provides him with the qualifications and skills to serve on our board of directors.

*Joel S. Marcus* has served as a member of our board of directors since June 2015. Mr. Marcus founded Alexandria Real Estate Equities, Inc., a real estate investment trust, and currently serves as Executive Chairman after previously serving as its Chairman since May 2007, Chief Executive Officer since March 1997 and a director since its founding in 1994. Mr. Marcus also co-founded and leads Alexandria Venture Investments, LLC which is a strategic venture arm of Alexandria Real Estate Equities, Inc. and the managing member of a holder of more than 5% of our outstanding shares. Prior to founding Alexandria Real Estate Equities, Inc., Mr. Marcus specialized in corporate finance and capital markets, venture capital and mergers and acquisitions with special expertise in the biopharmaceutical industry. Mr. Marcus received a B.A. and a J.D. from the University of California, Los Angeles. Our board of directors believes that Mr. Marcus' extensive experience in the life science real estate industry and as a chief executive officer, as well as his training as a C.P.A. and attorney, provide him with the qualifications and skills to serve on our board of directors.

*Neil Mendoza* has served as a member of our board of directors since June 2015. In 1986, Mr. Mendoza founded the custom marketing and publishing agency Forward, subsequently renamed Bookmark Content and

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Communications, a subsidiary of WPP plc. Mr. Mendoza is the Chairman of Victoria Private Investment Office, a London-based investment advisory firm, which he joined in 2010. He received a M.A. in Geography from Oxford University. Our board of directors believes Mr. Mendoza's extensive experience with investments provides him with the qualifications and skills to serve on our board of directors.

*Gregory S. Moss* has served as a member of our board of directors since May 2018. Mr. Moss joined Kadmon Holdings, Inc. in 2012 and has served as its Senior Vice President and Deputy General Counsel since 2012. He was also Acting General Counsel and Compliance Officer of MeiraGTx Limited from April 2015 to December 2016. He received a combined Bachelor of Arts and Bachelor of Laws degree from Macquarie University in 2007. Our board of directors believes Mr. Moss' experience serving as general counsel of a biopharmaceutical company provides him with qualifications and skills to serve on our board of directors.

*Thomas E. Shenk, Ph.D.* has served as a member of our board of directors since June 2015. Dr. Shenk has been the James A. Elkins Jr. Professor of Life Sciences in the Department of Molecular Biology at Princeton University since 1984. He received a B.S. from University of Detroit and a Ph.D. from Rutgers University. Dr. Shenk served on the board of directors of Merck and Co. Inc., a pharmaceutical company from 2001 to 2012. Dr. Shenk currently serves as a director of Vical Incorporated, a biopharmaceutical company, and Kadmon Holdings, Inc., a biopharmaceutical company. Our board of directors believes Dr. Shenk's expertise and experience serving as a director in the pharmaceutical sector and his academic background provides him with the qualifications and skills to serve on our board of directors.

### **Family Relationships**

There are no family relationships among any of our directors or executive officers.

### **Board Composition and Election of Directors**

#### ***Director Independence***

Our board of directors currently consists of nine members. Our board of directors has determined that, of our nine directors, \_\_\_\_\_, \_\_\_\_\_, and \_\_\_\_\_ do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of The Nasdaq Stock Market LLC, or Nasdaq. The listing requirements of Nasdaq, "independent directors" must comprise a majority of our board of directors within one year of closing of this offering.

#### ***Classified Board of Directors***

In accordance with our new articles of association that will go into effect upon the closing of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of shareholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. The election of directors will be by plurality of votes cast by the shareholders entitled to vote. Effective upon the closing of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be \_\_\_\_\_, \_\_\_\_\_, and \_\_\_\_\_, and their terms will expire at our first annual meeting of shareholders following this offering;
- the Class II directors will be \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_, and their terms will expire at our second annual meeting of shareholders following this offering; and
- the Class III directors will be \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_, and their terms will expire at the third annual meeting of shareholders following this offering.

Our new articles of association that will go into effect upon the closing of this offering will provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control of our company.

### ***Board Leadership Structure***

Our board of directors is currently chaired by . Our corporate governance guidelines provide that, if the chairman of the board is a member of management or does not otherwise qualify as independent, the independent directors of the board may elect a lead director. currently serves as our lead director. The lead director's responsibilities include, but are not limited to: presiding over all meetings of the board of directors at which the chairman is not present, including any executive sessions of the independent directors; approving board meeting schedules and agendas; and acting as the liaison between the independent directors and the chief executive officer and chairman of the board. Our corporate governance guidelines further provide the flexibility for our board of directors to modify our leadership structure in the future as it deems appropriate.

### **Role of the Board in Risk Oversight**

One of the key functions of our board of directors is informed oversight of our risk management process. Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure and our audit committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. Our audit committee also monitors compliance with legal and regulatory requirements. Our nominating and corporate governance committee monitors the effectiveness of our corporate governance practices, including whether they are successful in preventing illegal or improper liability-creating conduct. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, our entire board of directors is regularly informed through committee reports about such risks.

### **Board Committees**

Our board of directors has established three standing committees—audit, compensation and nominating and corporate governance—each of which operates under a charter that has been approved by our board of directors. Upon our listing on the Nasdaq Global Market, each committee's charter will be available under the "Corporate Governance" section of our website at [www.meirgtx.com](http://www.meirgtx.com). The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

### ***Audit Committee***

The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;

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- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- coordinating our board of directors' oversight of our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- discussing our risk management policies;
- meeting independently with our internal auditing staff, if any, registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by Securities Exchange Commission, or SEC, rules.

The members of our audit committee are \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_ serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable listing rules of Nasdaq, or Nasdaq rules. Our board of directors has determined that \_\_\_\_\_ and \_\_\_\_\_ meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable Nasdaq rules. Our board of directors has determined that \_\_\_\_\_ is an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules.

### ***Compensation Committee***

The compensation committee's responsibilities include:

- reviewing and approving, or recommending for approval by the board of directors, the compensation of our CEO and our other executive officers;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis," to the extent required; and
- preparing the annual compensation committee report required by SEC rules, to the extent required.

The members of our compensation committee are \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_ serves as the chairperson of the committee. Our board of directors has determined that each of \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_ is independent under the applicable Nasdaq rules, including the Nasdaq rules specific to membership on the compensation committee, and is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act.

### ***Nominating and Corporate Governance Committee***

The nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become board members;

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- recommending to our board of directors the persons to be nominated for election as directors and to each board committee;
- developing and recommending to our board of directors corporate governance guidelines, and reviewing and recommending to our board of directors proposed changes to our corporate governance guidelines from time to time; and
- overseeing a periodic evaluation of our board of directors.

The members of our nominating and corporate governance committee are \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_. \_\_\_\_\_ serves as the chairperson of the committee. Our board of directors has determined that \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_ are independent under the applicable Nasdaq rules.

### ***Compensation Committee Interlocks and Insider Participation***

No member of our compensation committee is or has been our current or former officer or employee. None of our executive officers served as a director or a member of a compensation committee (or other committee serving an equivalent function) of any other entity, one of whose executive officers served as a director or member of our compensation committee during the fiscal year ended December 31, 2017.

### **Code of Ethics and Code of Conduct**

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Upon our listing on the Nasdaq Global Market, our code of business conduct and ethics will be available under the “Corporate Governance” section of our website at [www.meiragtx.com](http://www.meiragtx.com). In addition, we intend to post on our website all disclosures that are required by law or the Nasdaq rules concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.



**EXECUTIVE AND DIRECTOR COMPENSATION****Executive Compensation**

This section discusses the material components of the executive compensation program for our executive officers who are named in the “2017 Summary Compensation Table” below. In 2017, our “named executive officers” and their positions were as follows:

- Alexandria Forbes, Ph.D., President and Chief Executive Officer;
- Richard Giroux, Chief Operating Officer; and
- Stuart Naylor, Ph.D., Chief Development Officer.

This discussion may contain forward-looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt following the completion of this offering may differ materially from the currently planned programs summarized in this discussion.

**2017 Summary Compensation Table**

The following table sets forth information concerning the compensation of our named executive officers for the year ended December 31, 2017.

<b>Name and Principal Position</b>	<b>Year</b>	<b>Salary (\$)</b>	<b>Bonus (\$)(1)</b>	<b>Option Awards (\$)(2)</b>	<b>All Other Compensation (\$)(3)</b>	<b>Total (\$)</b>
Alexandria Forbes, Ph.D. President and Chief Executive Officer	2017	450,000	490,000	165,969	16,200	1,122,169
Richard Giroux Chief Operating Officer	2017	400,000	440,000	153,202	—	993,202
Stuart Naylor, Ph.D. (4) Chief Development Officer	2017	257,800	528,900	25,534	25,780	838,014

(1) For Dr. Forbes and Mr. Giroux, amounts reflect a bonus accrued in 2017 and paid in early 2018 in connection with our achieving a fundraising milestone. For Dr. Naylor, amount reflects a \$400,000 discretionary bonus paid in the first quarter of 2018 attributable to performance in 2017 and \$128,900 accrued in 2017 and paid in early 2018 in connection with our achieving a fundraising milestone.

(2) Amounts reflect the full grant-date fair value of options granted during 2017 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of all option awards made to executive officers in Note 10 to our consolidated financial statements included elsewhere in this prospectus.

(3) Amounts shown represent employer contributions to our 401(k) plan for Dr. Forbes and a defined contribution pension scheme in the UK for Dr. Naylor.

(4) Amounts shown for Dr. Naylor were paid in pounds sterling and converted to U.S. dollars based on an average exchange rate for 2017 of \$1.289 to £1.00.

**Narrative to Summary Compensation Table****Base Salaries**

The named executive officers receive a base salary to compensate them for services rendered to our company. The base salary payable to each named executive officer is intended to provide a fixed component of compensation reflecting the executive’s skill set, experience, role and responsibilities.

Pursuant to the terms of their employment agreements, the base salaries of Dr. Forbes and Mr. Giroux were initially set at \$390,000 and \$320,000, respectively, and were increased to \$450,000 and \$400,000,

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respectively, in April 2016, in connection with our attaining a fundraising milestone. In addition, the base salaries of Dr. Forbes and Mr. Giroux were subsequently increased to \$580,000 and \$495,000, respectively, in connection with our attaining a second fundraising milestone in March 2018.

Dr. Naylor received an initial annual base salary of £200,000 pursuant to the terms of his employment agreement. His annual base salary was increased to £275,000 in January 2018.

### *Bonuses*

Dr. Forbes and Mr. Giroux are entitled to guaranteed annual cash bonus payments and may receive performance-based bonuses pursuant to the terms of their employment agreements, as described in more detail below under “Executive Compensation Arrangements—Dr. Forbes and Mr. Giroux.” In January 2018, the compensation committee determined that the guaranteed and performance based bonus amounts payable to Dr. Forbes and Mr. Giroux for 2017 would be \$1,078,000 and \$968,000, respectively, and that these amounts would be paid only upon the company’s satisfaction of performance milestones relating to (i) receipt of grant funds exceeding a threshold amount, (ii) equity investments or other upfront payments resulting in a cash balance above a threshold amount or (iii) the closing of an initial public offering. Consequently, Dr. Forbes and Mr. Giroux will become entitled to these bonus payments no later than the closing of this offering. In addition, in January 2018, Dr. Forbes and Mr. Giroux were paid bonuses that accrued in 2017 in connection with our achieving a fundraising milestone. These bonuses are included in the “bonus” column of the 2017 Summary Compensation Table above.

Pursuant to his employment agreement, Dr. Naylor has the opportunity to earn an annual discretionary bonus. In January 2018 the compensation committee determined to pay Dr. Naylor a bonus for 2017 performance of \$400,000.

### *Equity Compensation*

Our named executive officers currently hold restricted ordinary shares and options to purchase ordinary shares. In September 2017, the named executive officers were granted options as set forth below. The options generally vest as to 25% of the shares subject to the option on the first anniversary of the grant date and in 36 substantially equal monthly installments thereafter.

Pursuant to their employment agreements, Dr. Forbes and Mr. Giroux are entitled to annual grants of restricted ordinary shares in amounts as determined by the compensation committee with respect to Dr. Forbes or by our chief executive officer with respect to Mr. Giroux. For 2017, the compensation committee, with respect to Dr. Forbes, and the chief executive officer, with respect to Mr. Giroux, determined not to make any such grants.

The following table sets forth the options granted to our named executive officers in the 2017 fiscal year.

<u>Named Executive Officer</u>	<u>2017 Options Granted</u>
Alexandria Forbes, Ph.D.	325,000
Richard Giroux	300,000
Stuart Naylor, Ph.D	50,000

In January 2018, the named executive officers were granted options to purchase our ordinary shares in the following amounts: Dr. Forbes 400,000, Mr. Giroux 375,000 and Dr. Naylor 350,000. The options vest in accordance with our standard vesting schedule described above.

Dr. Forbes and Mr. Giroux are also entitled to certain equity-based incentive awards upon our achievement of certain corporate or financial milestones as set forth in their employment agreements. In

connection with our attaining a fundraising milestone on March 1, 2018, each of Dr. Forbes and Mr. Giroux became entitled to a grant of fully vested shares in an amount equal to 1.5% of our outstanding shares on a fully diluted basis plus payment of any associated income taxes incurred by the named executive officer. In March 2018, we issued each of Dr. Forbes and Mr. Giroux 1,067,591 vested ordinary shares and paid \$1,680,101 for the associated taxes incurred by each of Dr. Forbes and Mr. Giroux.

On the first to occur of the effectiveness of the registration statement of which this prospectus forms a part and a change in control, each of Dr. Forbes and Mr. Giroux is also entitled to a grant of restricted shares in an amount equal to 2.5 % of our outstanding shares on a fully diluted basis, which we refer to as the 2.5% award. One-third of the restricted shares subject to the 2.5% award will be vested at grant and the remaining shares will vest in eight quarterly installment over the two year period following the grant date. We currently expect to issue to Dr. Forbes and Mr. Giroux vested shares and restricted shares in respect of the 2.5% award on the date the registration statement of which this prospectus forms a part becomes effective. Pursuant to the terms of their employment agreements, the company will satisfy any taxes incurred by Dr. Forbes or Mr. Giroux in connection with the 2.5% award.

In connection with this offering, we intend to adopt a 2018 Incentive Award Plan, referred to below as the 2018 Plan, in order to facilitate the grant of cash and equity incentives to directors, employees (including our named executive officers) and consultants of our company and certain of its affiliates and to enable our company and certain of its affiliates to obtain and retain services of these individuals, which is essential to our long-term success. Following the effectiveness of the 2018 Plan, we will not make any further grants under the MeiraGTx Limited 2016 Equity Incentive Plan, referred to below as the 2016 Plan, under which we have previously made grants of equity and equity-based awards to our named executive officers and other key employees. For additional information about the 2018 Plan and the 2016 Plan, please see the section titled “Incentive Plans” below.

#### *Other Elements of Compensation*

##### *Retirement Plans*

We maintain a 401(k) retirement savings plan for our employees employed in the United States who satisfy certain eligibility requirements and contribute to defined contribution pension schemes on behalf of our employees employed in the United Kingdom. Our named executive officers are eligible to participate in our 401(k) plan in the United States and receive pension contributions in the United Kingdom on the same terms as other full-time employees in the applicable jurisdiction. We match 100% of employee contributions to our 401(k) plan, up to 6% of eligible compensation. We believe that providing a vehicle for tax-deferred retirement savings adds to the overall desirability of our executive compensation package and further incentivizes our employees, including our named executive officers, in accordance with our compensation policies.

##### *Employee Benefits*

All of our full-time employees, including our named executive officers, are eligible to participate in our health and welfare plans, subject to the same terms and eligibility requirements.

### Outstanding Equity Awards at Fiscal Year-End

The following table summarizes the number of ordinary shares underlying outstanding equity incentive plan awards for each named executive officer as of December 31, 2017.

Name	Grant Date	Option Awards				Stock Awards	
		Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable (1)	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)(2)	Market Value of Shares or Units of Stock That Have Not Vested (\$)
Alexandria Forbes, Ph.D.	3/4/2016	102,813	132,187	1.99	3/4/2026	—	—
	9/20/2017	—	325,000	0.68	9/20/2027	—	—
Richard Giroux	3/4/2016	83,125	106,875	1.99	3/4/2026	—	—
	9/20/2017	—	300,000	0.68	9/20/2027	—	—
Stuart Naylor, Ph.D.	4/24/2015	—	—	—	—	99,622	144,452
	3/4/2016	43,750	56,250	1.99	3/4/2026	—	—
	9/20/2017	—	50,000	0.68	9/20/2027	—	—

- (1) The options vest as to 25% of the total shares underlying the option on the first anniversary of the grant date and in equal monthly installments over the ensuing 36 months, subject to the holder's continued employment with us through the applicable vesting date and, for Dr. Forbes and Mr. Giroux, accelerated vesting upon a qualifying termination of employment as described in more detail below under "Executive Compensation Arrangements—Dr. Forbes and Mr. Giroux."
- (2) The restricted shares vest ratably on a daily basis over three years ending April 24, 2018.

### Executive Compensation Arrangements

We have entered into employment agreements with each of our named executive officers. Certain key terms of these agreements are described below.

#### *Dr. Forbes and Mr. Giroux*

We entered into employment agreements with Dr. Forbes and Mr. Giroux in February 2016. The agreements have an initial term of three years and automatically renew for successive one year periods unless notice of non-renewal is provided by either party at least 90 days prior to the expiration of the then-current term.

Pursuant to the employment agreements, Dr. Forbes and Mr. Giroux are entitled to annual base salaries in the amounts described above under "Base Salaries," annual cash bonuses equal to 100% of their respective base salaries, referred to as the guaranteed bonus, and the opportunity to earn annual performance-based bonuses targeted at 60% of base salary for Dr. Forbes and 50% of base salary for Mr. Giroux, referred to as the performance bonus.

In the event we complete a strategic collaboration resulting in upfront payments to us, each of Dr. Forbes and Mr. Giroux is entitled to a cash bonus in an amount determined by the compensation committee and, with respect to Mr. Giroux, the chief executive officer, provided that such bonus will not be less than 1% of the upfront payments received by us in such collaboration. There is no limit on the number of bonuses the executives may receive per year pursuant to this arrangement.

In the event either of Dr. Forbes's or Mr. Giroux's employment is terminated due to death or disability, or Dr. Forbes or Mr. Giroux resigns employment without good reason, which includes the executive's election not to renew the term of the employment agreement, the executive (or the executive's estate or beneficiary) is entitled to receive the executive's base salary, guaranteed bonus, and performance bonus as if the executive's employment had continued for an additional 12-month period.

In the event either of Dr. Forbes or Mr. Giroux is terminated by us for any reason other than cause, including due to a change in control, the company elects not to renew the term of the employment agreement, or

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Dr. Forbes or Mr. Giroux resigns for good reason, the executive is entitled to (i) three months' notice of termination or pay in lieu of notice, (ii) receive the executive's base salary, guaranteed bonus, and performance bonus as if the executive's employment had continued for an additional 24 month period (including a pro-rated guaranteed bonus and performance bonus for any stub periods), (iii) employee benefits and post-employment employee benefits and conversion rights in accordance with the terms and conditions of the plans, policies, programs, or perquisites in which the executive participates for a period of 24 months following the end of the then-current term, (iv) incentive and deferred compensation incentive rights in accordance with the terms and conditions of the incentive and deferred compensation plans in which the executive participates; provided, however, that the executive shall be deemed fully vested in any incentive and deferred compensation awards under such plans upon a termination, (v) accelerated vesting of any unvested restricted shares and equity incentive awards, (vi) to the extent not yet granted, be granted fully vested ordinary shares for the restricted shares provided for under the 2.5% award or other awards to which the executive may at the time be entitled as if all conditions applicable to such award were met, and (vii) be paid, within 30 days of termination, a cash termination fee equivalent to 1.50% for Dr. Forbes, or 1% for Mr. Giroux, of the average "market value" of our shares during the 90-trading day period prior to the termination plus payment of any taxes owed by the executive as a result of such termination fee. For purposes of the employment agreements, "market value" means the number obtained by multiplying (x) the aggregate number of shares of our voting and non-voting common equity (including stock held by employees and affiliates) by (y) the average of the last closing prices of our common equity in the principal market for such common equity, as adjusted on a pro-rata basis for any mechanical adjustments in our equity resulting from forward or reverse stock splits.

For purposes of the employment agreements, "cause" means the executive's (i) conviction of a felony involving moral turpitude, (ii) embezzlement, or (iii) intentional and willful misconduct that may subject us to criminal liability, which misconduct is not cured within 30 days after written notice to the executive of such conduct, if curable.

For purposes of the employment agreements, "good reason" means (i) any material diminution of the executive's title, duties, work responsibilities, authority, or status, or the assignment of duties that would typically be performed by someone in the executive's position to an individual other than the executive, (ii) a material negative change in the executive's reporting structure, (iii) a change in control, (iv) a reduction in the executive's then current base salary, (v) a change in the executive's principal place of employment to a location more than 15 miles from Manhattan, New York, (vi) our breach of the employment agreement that is not cured within 30 days after receiving notice of such breach, (vii) our insistence that the executive perform or condone any illegal conduct, or (viii) a hostile or abusive work environment or harassment.

### ***Dr. Naylor***

We have entered into an employment agreement with Dr. Naylor, pursuant to which he serves as our Chief Development Officer. The agreement is for an unspecified term and may be terminated by either party upon no less than 12-months' notice, or pay in lieu of notice.

Pursuant to his employment agreement, Dr. Naylor received an initial annual base salary of £200,000, which was increased to £275,000 in January 2018, and has the opportunity to earn discretionary annual bonuses.

Dr. Naylor's employment agreement contains certain restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting certain of our clients, customers or employees, in each case, for a period of 12 months following his termination of employment.

### **Director Compensation**

We provide our non-employee directors with meeting fees for each meeting of the board or committee attended, in person or telephonically. Non-employee directors receive \$4,000 (or \$6,000 for the chairman) for

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each meeting of the board attended in person and \$1,000 for each meeting of the board attended telephonically. Non-employee directors who are on committees of the board receive \$500 (or \$1,000 for the chairman of the committee) for each committee meeting attended in person or telephonically. Directors who are also employees of our company do not receive compensation for their service on our board.

In 2016, we granted certain non-employee directors options to purchase our ordinary shares. The options vested as to 50% of the shares upon grant and as to 50% of the shares on the first anniversary of the grant date. No options were granted to non-employee directors during 2017.

The following table sets forth information regarding the compensation of our non-employee directors earned during 2017:

<u>Name</u>	<u>Fees Earned or Paid in Cash (\$)</u>	<u>Total (\$)</u>
Thomas E. Shenk, Ph.D.	29,000	29,000
Keith R. Harris, Ph.D.	26,000	26,000
Ellen Hukkelhoven, Ph.D.	—	—
Arnold J. Levine, Ph.D.	23,000	23,000
Joel S. Marcus, J.D.	24,500	24,500
Neil Mendoza	21,500	21,500

The table below shows the aggregate numbers of option awards (exercisable and unexercisable) held as of December 31, 2017 by each non-employee director who was serving as of December 31, 2017.

<u>Name</u>	<u>Options Outstanding (#)</u>
Thomas E. Shenk, Ph.D.	75,000
Keith R. Harris, Ph.D.	50,000
Ellen Hukkelhoven, Ph.D.	—
Arnold J. Levine, Ph.D.	25,000
Joel S. Marcus, J.D.	50,000
Neil Mendoza	50,000

In January 2018, our non-employee directors were granted options to purchase our ordinary shares in the following amounts: Mr. Shenk 90,000, Mr. Harris 90,000, Mr. Mendoza 60,000, Mr. Marcus 60,000 and Mr. Levine 60,000. The options vest in full on the first anniversary of the grant date.

We intend to approve and implement a compensation program for our non-employee directors that consists of annual retainer fees and long-term equity awards. The material terms of this program are not yet known and will be described in this prospectus once they are determined.

### **Incentive Plans**

The following summarizes the material terms of the long-term incentive compensation plan in which our named executive officers will be eligible to participate following the consummation of this offering and the MeiraGTx Limited 2016 Equity Incentive Plan, or the 2016 Plan, under which we have previously made periodic grants of equity and equity-based awards to our named executive officers and other key employees.

#### ***MeiraGTx Limited 2016 Equity Incentive Plan***

Our board of directors approved the 2016 Plan under which we may grant non-qualified options, restricted stock, restricted stock units and other-stock based awards covering our ordinary shares. We had reserved a total of \_\_\_\_\_ ordinary shares for issuance under the 2016 Plan as of \_\_\_\_\_.

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Following the effectiveness of the 2018 Plan, we will not make any further grants under the 2016 Plan. However, the 2016 Plan will continue to govern the terms and conditions of the outstanding awards granted under it. Our ordinary shares subject to awards granted under the 2016 Plan that are forfeited, lapse unexercised or are settled in cash and which following the effective date of the 2018 Plan are not issued under the 2016 Plan will be available for issuance under the 2018 Plan.

Our board of directors administers the 2016 Plan and has the authority to take all actions and make all determinations under the 2016 Plan, and to adopt, amend and repeal rules for the administration of the 2016 Plan as it deems advisable. The board of directors may delegate its authority under the 2016 Plan to a committee of the board. Following the effectiveness of this offering, we expect that the board of directors will delegate its general administrative authority under the 2016 Plan to its compensation committee.

The 2016 Plan provides for the grant of non-qualified options, restricted stock, restricted stock units and other-stock based awards covering our ordinary shares to employees, directors and consultants of the company or its subsidiaries. As of the date of this prospectus, awards of options and restricted stock are outstanding under the 2016 Plan.

In connection with certain corporate transactions and events affecting our ordinary shares, including a change in control, or change in any applicable laws or accounting principles, the board of directors has broad discretion to take action under the 2016 Plan to prevent the dilution or enlargement of intended benefits, facilitate the transaction or event or give effect to the change in applicable laws or accounting principles. In addition, in the event of certain non-reciprocal transactions with our shareholders, the board of directors will make equitable adjustments to outstanding awards under the 2016 Plan as it deems appropriate to reflect the transaction.

The board of directors may amend, suspend or terminate the 2016 Plan, or any portion thereof, at any time; provided that no amendment may materially and adversely affect an outstanding award without the consent of the affected participant.

### **2018 Incentive Award Plan**

Effective the day prior to the first public trading date of our ordinary shares, we intend to adopt and ask our shareholders to approve the 2018 Incentive Award Plan, or the 2018 Plan, under which we may grant cash and equity-based incentive awards to eligible service providers in order to attract, retain and motivate the persons who make important contributions to our company. The material terms of the 2018 Plan are summarized below.

#### *Eligibility and Administration*

Our employees, consultants and directors, and employees and consultants of our subsidiaries, will be eligible to receive awards under the 2018 Plan. The 2018 Plan will be administered by our board of directors, which may delegate its duties and responsibilities to one or more committees of our directors and/or officers (referred to collectively as the plan administrator below), subject to the limitations imposed under the 2018 Plan, Section 16 of the Exchange Act, stock exchange rules and other applicable laws. The plan administrator will have the authority to take all actions and make all determinations under the 2018 Plan, to interpret the 2018 Plan and award agreements and to adopt, amend and repeal rules for the administration of the 2018 Plan as it deems advisable. The plan administrator will also have the authority to determine which eligible service providers receive awards, grant awards and set the terms and conditions of all awards under the 2018 Plan, including any vesting and vesting acceleration provisions, subject to the conditions and limitations in the 2018 Plan.

#### *Shares Available for Awards*

An aggregate of                      ordinary shares will initially be available for issuance under the 2018 Plan. The number of shares initially available for issuance will be increased by an annual increase on January 1 of each

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calendar year beginning in 2019 and ending in and including 2028, equal to the lesser of (A) \_\_\_\_\_, (B) \_\_\_\_\_ % of the ordinary shares outstanding on of the immediately preceding calendar year and (C) a smaller number of shares determined by our board of directors. No more than \_\_\_\_\_ ordinary shares may be issued under the 2018 Plan upon the exercise of incentive stock options. Shares issued under the 2018 Plan may be authorized but unissued shares, shares purchased on the open market or treasury shares.

If an award under the 2018 Plan or the 2016 Plan, expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any unused shares subject to the award will, as applicable, become or again be available for new grants under the 2018 Plan. Awards granted under the 2018 Plan in substitution for any options or other share or share-based awards granted by an entity before the entity's merger or consolidation with us or our acquisition of the entity's property or stock will not reduce the shares available for grant under the 2018 Plan, but will count against the maximum number of shares that may be issued upon the exercise of incentive stock options.

### *Awards*

The 2018 Plan provides for the grant of options, including incentive stock options, or ISOs, and nonqualified stock options, or NSOs, share appreciation rights, or SARs, restricted shares, dividend equivalents, restricted share units, or RSUs, and other share or cash based awards. Certain awards under the 2018 Plan may constitute or provide for payment of "nonqualified deferred compensation" under Section 409A of the Code. All awards under the 2018 Plan will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows.

- *Options and SARs.* Options provide for the purchase of our ordinary shares in the future at an exercise price set on the grant date. ISOs, by contrast to NSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding period and other requirements of the Code are satisfied. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The plan administrator will determine the number of shares covered by each option and SAR, the exercise price of each option and SAR and the conditions and limitations applicable to the exercise of each option and SAR. The exercise price of an option or SAR will not be less than 100% of the fair market value of the underlying share on the grant date (or 110% in the case of ISOs granted to certain significant shareholders), except with respect to certain substitute awards granted in connection with a corporate transaction. The term of an option or SAR may not be longer than ten years (or five years in the case of ISOs granted to certain significant shareholders).
- *Restricted Shares and RSUs.* A restricted share is an award of nontransferable ordinary shares that remain forfeitable unless and until specified conditions are met and which may be subject to a purchase price. RSUs are contractual promises to deliver ordinary shares in the future, which may also remain forfeitable unless and until specified conditions are met and may be accompanied by the right to receive the equivalent value of dividends paid on ordinary shares prior to the delivery of the underlying shares. The plan administrator may provide that the delivery of the shares underlying RSUs will be deferred on a mandatory basis or at the election of the participant. The terms and conditions applicable to restricted shares and RSUs will be determined by the plan administrator, subject to the conditions and limitations contained in the 2018 Plan.
- *Other Share or Cash Based Awards.* Other share or cash based awards are awards of cash, fully vested ordinary shares and other awards valued wholly or partially by referring to, or otherwise based on, our ordinary shares or other property. Other share or cash based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as



standalone payments and as payment in lieu of compensation to which a participant is otherwise entitled. The plan administrator will determine the terms and conditions of other share or cash based awards, which may include any purchase price, performance goal, transfer restrictions and vesting conditions.

#### *Performance Criteria*

The plan administrator may select performance criteria for an award to establish performance goals for a performance period. Performance criteria under the 2018 Plan may include, but are not limited to, the following: net earnings or losses (either before or after one or more of interest, taxes, depreciation, amortization, and non-cash equity-based compensation expense); gross or net sales or revenue or sales or revenue growth; net income (either before or after taxes) or adjusted net income; profits (including but not limited to gross profits, net profits, profit growth, net operation profit or economic profit), profit return ratios or operating margin; budget or operating earnings (either before or after taxes or before or after allocation of corporate overhead and bonus); cash flow (including operating cash flow and free cash flow or cash flow return on capital); return on assets; return on capital or invested capital; cost of capital; return on shareholders' equity; total shareholder return; return on sales; costs, reductions in costs and cost control measures; expenses; working capital; earnings or loss per share; adjusted earnings or loss per share; price per share or dividends per share (or appreciation in or maintenance of such price or dividends); regulatory achievements or compliance; implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; market share; economic value or economic value added models; division, group or corporate financial goals; customer satisfaction/growth; customer service; employee satisfaction; recruitment and maintenance of personnel; human resources management; supervision of litigation and other legal matters; strategic partnerships and transactions; financial ratios (including those measuring liquidity, activity, profitability or leverage); debt levels or reductions; sales-related goals; financing and other capital raising transactions; cash on hand; acquisition activity; investment sourcing activity; and marketing initiatives, any of which may be measured in absolute terms or as compared to any incremental increase or decrease. Such performance goals also may be based solely by reference to the company's performance or the performance of a subsidiary, division, business segment or business unit of the company or a subsidiary, or based upon performance relative to performance of other companies or upon comparisons of any of the indicators of performance relative to performance of other companies. When determining performance goals, the plan administrator may provide for exclusion of the impact of an event or occurrence which the plan administrator determines should appropriately be excluded, including, without limitation, non-recurring charges or events, acquisitions or divestitures, changes in the corporate or capital structure, events unrelated to the business or outside of the control of management, foreign exchange considerations, and legal, regulatory, tax or accounting changes.

#### *Certain Transactions*

In connection with certain corporate transactions and events affecting our ordinary shares, including a change in control, or change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under the 2018 Plan to prevent the dilution or enlargement of intended benefits, facilitate the transaction or event or give effect to the change in applicable laws or accounting principles. This includes canceling awards for cash or property, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor entity, adjusting the number and type of shares subject to outstanding awards and/or with respect to which awards may be granted under the 2018 Plan and replacing or terminating awards under the 2018 Plan. In addition, in the event of certain non-reciprocal transactions with our shareholders, the plan administrator will make equitable adjustments to the 2018 Plan and outstanding awards as it deems appropriate to reflect the transaction.

#### *Plan Amendment and Termination*

Our board of directors may amend or terminate the 2018 Plan at any time; however, no amendment, other than an amendment that increases the number of shares available under the 2018 Plan, may materially and

adversely affect an award outstanding under the 2018 Plan without the consent of the affected participant and shareholder approval will be obtained for any amendment to the extent necessary to comply with applicable laws. Further, the plan administrator cannot, without the approval of our shareholders, amend any outstanding option or SAR to reduce its price per share. The 2018 Plan will remain in effect until the tenth anniversary of its effective date, unless earlier terminated by our board of directors. No awards may be granted under the 2018 Plan after its termination.

*Non-US Participants, Claw-Back Provisions, Transferability and Participant Payments*

The plan administrator may modify awards granted to participants who are non-US nationals or employed outside the United States or establish subplans or procedures to address differences in laws, rules, regulations or customs of such jurisdictions outside the United States. All awards will be subject to any company claw-back policy as set forth in such claw-back policy or the applicable award agreement. Except as the plan administrator may determine or provide in an award agreement, awards under the 2018 Plan are generally non-transferrable, except by will or the laws of descent and distribution, or, subject to the plan administrator's consent, pursuant to a domestic relations order, and are generally exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under the 2018 Plan, and exercise price obligations arising in connection with the exercise of options under the 2018 Plan, the plan administrator may, in its discretion, accept cash, wire transfer or check, our ordinary shares that meet specified conditions, a promissory note, a "market sell order," such other consideration as the plan administrator deems suitable or any combination of the foregoing.

**2018 Employee Stock Purchase Plan**

Effective the day prior to the first public trading date of our ordinary shares, we intend to adopt and ask our shareholders to approve the 2018 Employee Share Purchase Plan, or the 2018 ESPP. The material terms of the 2018 ESPP are summarized below.

*Shares Available for Awards; Administration*

A total of \_\_\_\_\_ ordinary shares will initially be reserved for issuance under the 2018 ESPP. In addition, the number of shares available for issuance under the 2018 ESPP will be annually increased on January 1 of each calendar year beginning in 2019 and ending in and including 2028, by an amount equal to the least of (A) \_\_\_\_\_ % of the shares outstanding on the final day of the immediately preceding calendar year and (B) such smaller number of shares as is determined by our board of directors, provided that no more than \_\_\_\_\_ ordinary shares may be issued under the 2018 ESPP. The foregoing numbers are subject to adjustment in certain events, as described below. Our board of directors or a committee of our board of directors will have authority to interpret the terms of the 2018 ESPP and determine eligibility of participants. We expect that the compensation committee will be the initial administrator of the 2018 ESPP.

*Eligibility*

Our employees are eligible to participate in the 2018 ESPP if they are customarily employed by us or a participating subsidiary for more than twenty hours per week and more than five months in any calendar year. However, an employee may not be granted rights to purchase shares under our 2018 ESPP if the employee, immediately after the grant, would own (directly or through attribution) shares possessing 5% or more of the total combined voting power or value of all classes of our shares.

*Grant of Rights*

The 2018 ESPP is intended to qualify under Section 423 of the Code and shares will be offered under the 2018 ESPP during offering periods. The length of the offering periods under the 2018 ESPP will be

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determined by the plan administrator and may be up to twenty-seven months long. Employee payroll deductions will be used to purchase shares on each purchase date during an offering period. The purchase dates for each offering period will be the final trading day in the offering period. Offering periods under the 2018 ESPP will commence when determined by the plan administrator. The plan administrator may, in its discretion, modify the terms of future offering periods.

The 2018 ESPP permits participants to purchase ordinary shares through payroll deductions of up to \_\_\_\_\_ % of their eligible compensation, which includes a participant's gross base compensation for services to us, including overtime payments and excluding sales commissions, incentive compensation, bonuses, expense reimbursements, fringe benefits and other special payments. The plan administrator will establish a maximum number of shares that may be purchased by a participant during any offering period, which, in the absence of a contrary designation, will be \_\_\_\_\_ shares. In addition, no employee will be permitted to accrue the right to purchase shares under the 2018 ESPP at a rate in excess of \$25,000 worth of shares during any calendar year during which such a purchase right is outstanding (based on the fair market value per share of our ordinary shares as of the first day of the offering period).

On the first trading day of each offering period, each participant will automatically be granted an option to purchase our ordinary shares. The option will expire at the end of the applicable offering period, and will be exercised at that time to the extent of the payroll deductions accumulated during the offering period. The purchase price of the shares, in the absence of a contrary designation, will be 85% of the lower of the fair market value of our ordinary shares on the first trading day of the offering period or on the purchase date. Participants may voluntarily end their participation in the 2018 ESPP at any time at least one week prior to the end of the applicable offering period, and will be paid their accrued payroll deductions that have not yet been used to purchase ordinary shares. Participation ends automatically upon a participant's termination of employment.

A participant may not transfer rights granted under the 2018 ESPP other than by will or the laws of descent and distribution.

### *Certain Transactions*

In the event of certain non-reciprocal transactions or events affecting our ordinary shares known as "equity restructurings," the plan administrator will make equitable adjustments to the 2018 ESPP and outstanding rights. In the event of certain unusual or non-recurring events or transactions, including a change in control, the plan administrator may provide for (1) either the replacement of outstanding rights with other rights or property or termination of outstanding rights in exchange for cash, (2) the assumption or substitution of outstanding rights by the successor or survivor corporation or parent or subsidiary thereof, if any, (3) the adjustment in the number and type of shares subject to outstanding rights, (4) the use of participants' accumulated payroll deductions to purchase shares on a new purchase date prior to the next scheduled purchase date and termination of any rights under ongoing offering periods or (5) the termination of all outstanding rights.

### *Plan Amendment*

The plan administrator may amend, suspend or terminate the 2018 ESPP at any time. However, shareholder approval will be obtained for any amendment that increases the aggregate number or changes the type of shares that may be sold pursuant to rights under the 2018 ESPP, changes the corporations or classes of corporations whose employees are eligible to participate in the 2018 ESPP or changes the 2018 ESPP in any manner that would cause the 2018 ESPP to no longer be an employee stock purchase plan within the meaning of Section 423(b) of the Code.

## CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following includes a summary of transactions since January 1, 2015 to which we have been a party in which the amount involved exceeded or will exceed \$120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our share capital or any member of the immediate family of any of the foregoing persons had, or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under “Executive and Director Compensation.” We also describe below certain other transactions with our directors, executive officers and shareholders.

### **Preferred and Ordinary Share Financings**

#### ***Series C Preferred Shares***

From October 2015 through April 2018, we issued an aggregate 39,480,891 Series C preferred shares at a purchase price of \$2.70 per share, for aggregate consideration of approximately \$106.6 million, to investors.

From April 2016 to September 2017, we issued an aggregate 460,000 Series C preferred shares to Kadmon Corporation, LLC, or Kadmon, with an aggregate value of approximately \$1.2 million as partial payment of amounts owed under the transition services agreement, or Kadmon TSA. See “—Kadmon Transition Services Agreement” for additional information.

In May 2017, we issued a convertible note to an entity affiliated with Alexandria Equities, No. 7, LLC, or Alexandria, in the principal amount of \$2.5 million and an interest rate of 10% per annum, or the Convertible Note. In November 2017, we issued 925,926 Series C preferred shares to Alexandria, with an aggregate value of approximately \$2.5 million, upon conversion of the Convertible Note in satisfaction of the full principal. In accordance with the terms of the Convertible Note, the accrued interest in an amount of \$0.1 million was cancelled.

#### ***Warrants***

In September 2017, we issued a warrant to Perceptive Life Sciences Master Fund, Ltd., to purchase 2,700,000 of our Series C preferred shares at an exercise price of \$2.70, which was valued under the Black-Scholes pricing model at approximately \$1.7 million.

In November 2017, we issued a warrant to Alexandria to purchase 900,000 Series C preferred shares at an exercise price of \$2.70, which was valued under the Black-Scholes pricing model at approximately \$0.6 million, as an inducement to convert the Convertible Note described above.

#### ***Series A Ordinary Shares***

In April 2015, we issued an aggregate of 4,078,320 Series A ordinary shares of purchase prices of \$2.00 and \$3.50 per share, for an aggregate consideration of approximately \$8.7 million to investors and an aggregate of 21,779,382 Series A ordinary shares for nominal consideration to our founders.

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The following table sets forth the aggregate number of Series A ordinary shares, Series C preferred shares and warrants to purchase Series C preferred shares acquired by directors and officers and beneficial owners of more than 5% of our shares in the financing transactions described above.

<u>Participants</u>	<u>Series A Ordinary Shares</u>	<u>Series C Preferred Shares</u>	<u>Warrants</u>
<b>Directors and Officers</b>			
Alexandria Forbes†	3,320,871	—	—
Richard Giroux†	2,219,271	—	—
Stuart Naylor	1,982,807	—	—
Thomas Shenk	662,910	—	—
Gregory S. Moss	160,230	—	—
Joel S. Marcus	125,000	185,180	—
Neil Mendoza	50,000	—	—

† Indicates a Founder

<u>Participants</u>	<u>Series A Ordinary Shares</u>	<u>Series C Preferred Shares</u>	<u>Warrants</u>
<b>5% or Greater Shareholders(1)</b>			
Kadmon Corporation, LLC	13,258,200	460,000	—
Perceptive Life Sciences Master Fund, Ltd	—	10,185,186	2,700,000
Adena Estate, Inc.	1,250,000	5,555,556	—
Alexandria Equities No. 7, LLC	374,500	5,126,809	900,000
Robin Ali Ph.D.†	4,246,808	—	—

(1) Additional details regarding these shareholders and their equity holdings are provided in this prospectus under the caption “Principal Shareholders.”

† Indicates a Founder

Some of our directors are associated with our principal shareholders as indicated in the table below:

<u>Director</u>	<u>Principal Shareholder</u>
Alexandria Forbes	Kadmon Corporation, LLC
Thomas E. Shenk	Kadmon Corporation, LLC
Gregory S. Moss	Kadmon Corporation, LLC
Ellen Hukkelhoven	Perceptive Life Sciences Master Fund, Ltd
Joel S. Marcus	Alexandria Equities No. 7, LLC

## **License Agreements**

In February 2015, Athena Vision Ltd., an entity acquired in April 2016, entered into a license agreement with UCL Business, PLC, or UCLB, which was amended in March 2015, July 2017 and December 2017. See “Business—Licensed Intellectual Property.”

In May 2013, BRI-Alzan Inc. entered into a license agreement that was assigned to us as a result of our subsequent merger with BRI-Alzan Inc. in 2015. See “Business—Licensed Intellectual Property.”

## **Employment Agreements**

We have entered into employment agreements with our named executive officers. For more information regarding the agreements with our named executive officers, see “Executive and Director Compensation—Executive Compensation Arrangements.”

In April 2015, we entered into a service agreement with Robin Ali, a greater than 5% holder of our ordinary shares. On April 24, 2015, we granted Dr. Ali pursuant to the service agreement 1,739,300 Series A

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ordinary shares. Under the terms of the agreement, Dr. Ali will receive aggregate compensation of £110,000 per year, or approximately \$146,000 using average exchange rates as of December 31, 2017. The agreement may be terminated at any time by either party by giving twelve-months' notice. For the years ended December 31, 2015, 2016 and 2017, the Company recorded £110,000, £110,000 and £110,000 or approximately \$162,000, \$135,000 and \$128,000, respectively, using the average exchange rates during the year ended December 31, 2015, 2016 and 2017, respectively, in research and development costs under these agreements. Future obligations to be paid under this agreement equal £110,000, or approximately \$149,000, using exchange rates as of December 31, 2017.

In April 2015, we entered into a service agreement with Stuart Naylor, one of our officers and directors. On April 24, 2015, we granted Mr. Naylor pursuant to the service agreement 966,250 Series A ordinary shares. For further information, see "Executive and Director Compensation—Executive Compensation Arrangements.

### **Consulting Agreements**

We and Samuel D. Waksal, Ph.D., a holder of 7.8% of our outstanding equity at the time of our formation in March 2015, and therefore a "related person" under Item 404 of Regulation S-K, entered into a consulting agreement on April 24, 2015 that was subsequently renewed on January 1, 2016, January 1, 2017 and January 1, 2018. Pursuant to the terms of the consulting agreement, we paid Dr. Waksal compensation for his consulting services of \$750,000, \$850,000 and \$850,000 for each of the years ended December 31, 2015, December 31, 2016, and December 31, 2017, respectively. Effective On May 14, 2018, we terminated Dr. Waksal's agreement, and pursuant to its terms, we have agreed to pay him compensation of \$197,260.27 for services performed during 2018. In addition, on March 4, 2016 and September 20, 2017, Dr. Waksal was granted options to purchase 200,000 and 300,000 ordinary shares, respectively, at exercise prices of \$1.99 and \$0.68, respectively. In 2002, Dr. Waksal was charged by the SEC with violating the federal securities laws in connection with trades made in the shares of ImClone Systems Incorporated, where he served as president and chief executive officer and as a director. Dr. Waksal was also charged with, and subsequently pled guilty to, securities fraud, bank fraud, wire fraud, obstruction of justice, perjury and related conspiracy charges. He is subject to a final judgment and order on consent that permanently bars him from acting as an officer or director of any public company. As of April 30, 2018, Dr. Waksal held shares representing approximately 2.9% of our outstanding equity. Upon completion of this offering, Dr. Waksal will hold shares representing approximately % of our outstanding equity, assuming that we sell the number of shares set forth on the cover page of this prospectus in this offering.

Effective September 28, 2015, we entered into a three-year consulting agreement with Thomas Shenk, Ph.D., one of our directors. In connection with the agreement, we issued Dr. Shenk 662,910 Series A ordinary shares for aggregate consideration of \$1.3 million. Under the consulting agreement, such shares are subject to forfeiture ratably over a period of three years if Dr. Shenk does not remain a consultant to us.

### **Indemnification Agreements**

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer against all expenses such as attorneys' fees, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by the director or executive officer or on his behalf, in connection with such proceeding or any claim, issue or matter therein, if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of our company, and with respect to any criminal proceeding, had no reasonable cause to believe the person's conduct was unlawful. For further information, see "Executive and Director Compensation—Limitations of Liability and Indemnification."

### **Share Option and Restricted Share Grants to Executive Officers and Directors**

We have granted share options and restricted shares to our executive officers and certain of our directors as more fully described in the section entitled "Executive and Director Compensation."

### **Kadmon Transition Services Agreement**

In April 2015, we entered into the Kadmon TSA to provide us with office and laboratory facilities, as well as personal support activities. Under the agreement, we are charged for (i) rent based upon the square footage of the office and laboratory facilities we use, (ii) other personnel support activities based upon hours of the personnel providing the support activities, and (iii) other direct costs incurred by Kadmon on our behalf, plus a 7% administrative fee. We made cash payments under the agreement of \$225,078 and \$275,941 during the years ended December 31, 2016 and 2017, respectively. During the three-month periods ended March 31, 2017 and 2018, we made cash payments to Kadmon totaling \$275,941 and \$997,417, respectively. From April 2016 to September 2017, we issued an aggregate 460,000 Series C preferred shares to Kadmon in aggregate amount of \$1,242,000 as partial payment of amounts owed under the agreement. As of December 31, 2016 and 2017 and March 31, 2018, the amount due to Kadmon was \$543,038, \$861,030 and \$6,493, respectively. Either party may terminate the agreement upon 30-days' notice.

### **Moorfields Lease**

In February 2016, we entered into a five-year lease with Moorfields Eye Hospital, NHS Foundation Trust and Kadmon, a greater than 5% shareholder. Under the lease, Kadmon is a guarantor of our rent obligations and has agreed to indemnify Moorfields as the landlord against any failure by the tenant to pay the rent or otherwise perform its obligations thereunder.

### **UCL Agreements**

#### ***Services Agreement***

In October 2016, we entered into a four-year services agreement with UCL Consultants Limited, an entity affiliated with UCLB. One of our shareholders, Robin Ali, is a professor at University College London, or UCL, an entity affiliated with UCLB and UCL Consultants Limited. Under the agreement, UCL Consultants Limited provides pre-clinical research and development services under our direction. In connection with the agreement, we issued several work orders during the years ended December 31, 2016 and 2017 in aggregate amounts of \$1,574,000 and \$311,000, respectively. The total research and development expenses for the years ended December 31, 2016 and 2017 were approximately \$278,000 and \$538,000, respectively. Future obligations under the agreement are approximately \$1,438,869. As of the years ended December 31, 2016 and 2017, the amount due to UCL was \$251,754 and \$775,315, respectively. Either party may terminate the agreement upon 30-days written notice.

#### ***Manufacturing and Supply Agreement***

In September 2016, we entered into a manufacturing and drug supply agreement with UCL to manufacture materials for our clinical trials under our direction, which was terminated in January 2018. The total research and development expenses for the years ending December 31, 2016 and 2017 were \$456,106 and \$1,904,352, respectively. As of the years ended December 31, 2016 and 2017, the amount due to UCL was \$412,395 and \$2,466,142, respectively.

### **ARE Leases**

#### ***July 2016 Lease***

Effective July 2016, we entered into a non-cancellable operating lease for laboratory facilities in New York with ARE-East River Science Park, LLC, or ARE, an entity affiliated with Alexandria and Joel S. Marcus, Executive Chairman of Alexandria Real Estate Equities, Inc. Under the lease, we pay monthly base rent, property management fees and operating expenses for the duration of the lease term, which expires in December 2021. The total rent expense under the lease for the years ended December 31, 2016 and 2017 was \$243,780 and \$487,559, respectively. In July 2016, in connection with the signing of the lease, we entered into a standby letter of credit agreement for \$122,866, which serves as a security deposit for the premises. The standby letter of credit

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expires on is automatically renewed annually through July 7, 2021. As of the years ended December 31, 2016 and 2017, the balance of deferred rent was \$243,780 and \$231,276, respectively. Aggregate future minimum rental payments under the lease are \$2,181,520 as of December 31, 2017.

### **December 2016 Lease**

In December 2016, we entered into a non-cancellable operating lease for laboratory and office facilities in New York with ARE expiring in October 2032. Under the lease, we pay monthly base rent, property management fees, and operating expenses during the lease term. In December 2016, in connection with the signing of the lease, we entered into a standby letter of credit agreement for \$321,977, which served as a security deposit for the premises. The standby letter of credit was cancelled on November 2017. In October 2017, the lease was amended whereby the lease would terminate on March 2018 and only base rent and management fees in the aggregate amount of \$563,507 would be due for the period from November 2017 through March 2018. Under the amendment, we issued a promissory note in the principal amount of \$1,442,009 to ARE at an interest rate of 5% per annum, which removed the balance of the deferred rent and accrued the future rent payments. The note is due on December 31, 2018, however, the note and accrued interest will become due and payable if we achieve sufficient liquidity as defined in the note. If we do not have sufficient liquidity, which is defined as our cash, cash equivalents and liquid short-term investments of at least an investment grade are at least 20 times greater than the note plus accrued interest, prior to the due date, we may repay the note in either cash or Series C preferred shares. We recorded an interest expense in the amount of \$13,037 for the year ended December 31, 2017. The total rent expense under the operating lease was \$43,578 and \$1,660,806 for the years ended December 31, 2016 and 2017 respectively. As of the years ended December 31, 2016 and 2017, the balance of deferred lease obligation was \$11,380 and \$0 respectively. Aggregate future minimal rental payments under the lease are \$332,442 as of December 31, 2017.

### **Shareholder Agreement**

Upon consummation of the Reorganization Transactions, we will enter into a Shareholder Agreement with our shareholders, including Alexandria Forbes, Richard Giroux, Stuart Naylor, Joel S. Marcus, Thomas Shenk, Keith Harris, Arnold Levine, Kadmon Corporation, LLC, Perceptive Life Sciences Master Fund, Ltd., Adena Estate, Inc., Alexandria Equities No. 7, LLC. and Robin Ali. The Shareholder Agreement, other than provisions related to registration rights, confidentiality, rights of third parties and governing law, will terminate upon consummation of our initial public offering. Provisions related to registration rights will terminate upon the earlier to occur of a deemed liquidation event, such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of a holder's shares without limitation during a three-month period without registration, and the third anniversary of our initial public offering. See "Description of Share Capital and Articles of Association-Registration Rights" for additional information.

### **Policies and Procedures for Related Person Transactions**

Our board of directors has adopted a written related person transaction policy, to be effective upon the closing of this offering, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, where the amount involved exceeds \$5,000 in any fiscal year and a related person had, has or will have a direct or indirect material interest, including without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.



## PRINCIPAL SHAREHOLDERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares, as of April 30, 2018, (i) immediately prior to this offering, and (ii) after giving effect to the offering, in each case after giving effect to our corporate reorganization:

- each person or group of affiliated persons known by us to beneficially own more than 5% of our ordinary shares;
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

The number of shares beneficially owned by each shareholder is determined under rules issued by the Securities and Exchange Commission. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. Applicable percentage ownership is based on 77,426,947 ordinary shares outstanding as of April 30, 2018, after giving effect to our corporate reorganization. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, ordinary shares subject to options, warrants or other rights held by such person that are currently exercisable or will become exercisable within 60 days of April 30, 2018 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless noted otherwise, the address of all listed shareholders is 430 E. 29<sup>th</sup> Street, 10<sup>th</sup> Floor, New York, New York 10016. Each of the shareholders listed has sole voting and investment power with respect to the shares beneficially owned by the shareholder unless noted otherwise, subject to community property laws where applicable.

<u>Name of Beneficial Owner</u>	<u>Shares Beneficially Owned Prior to Offering</u>		<u>Shares Beneficially Owned After Offering</u>	
	<u>Number</u>	<u>Percentage</u>	<u>Number</u>	<u>Percentage</u>
<b>5% or Greater Shareholders</b>				
Kadmon Corporation, LLC(1)	13,718,200	17.7%		%
Perceptive Life Sciences Master Fund, Ltd(2)	12,885,186	16.1		
Adena Estate, Inc.(3)	6,805,556	8.8		
Alexandria Equities No. 7, LLC(4)	6,401,309	8.2		
Robin Ali, Ph.D.(5)	4,246,808	5.5		
<b>Named Executive Officers and Directors</b>				
Keith R. Harris, Ph.D.(6)	50,000	*		
Alexandria Forbes, Ph.D.(7)	3,453,059	4.5		
Ellen Hukkelhoven, Ph.D.(2)	12,885,186	16.1		
Arnold J. Levine, Ph.D.(8)	25,000	*		
Joel S. Marcus(9)	6,761,489	8.6		
Neil Mendoza(10)	100,000	*		
Gregory S. Moss(11)	13,878,430	17.9		
Stuart Naylor, Ph.D.(12)	2,039,057	2.6		
Thomas E. Shenk, Ph.D.(13)	737,910	1.0		
Richard Giroux(14)	2,326,146	3.0		
All executive officers and directors as a group (10 persons)	42,256,277	53.9		

\* Less than 1%.

- (1) Consists of 13,718,200 ordinary shares. The sole member of Kadmon Corporation, LLC is Kadmon Holdings, Inc. Alexandria Forbes and Thomas Shenk, two of our directors, are also directors of Kadmon Holdings, Inc. and Gregory S. Moss, one of our directors, is Senior Vice President, Deputy General Counsel of Kadmon Holdings, Inc. The address of Kadmon Corporation, LLC is 450 E. 29<sup>th</sup> Street, 16<sup>th</sup> Floor, New York, New York 10016.
- (2) Consists of 10,185,186 ordinary shares and a warrant to purchase 2,700,000 ordinary shares that is or will be immediately exercisable within 60 days of April 30, 2018 held by Perceptive Life Sciences Master Fund, Ltd. Ellen Hukkelhoven, one of our directors, is a senior analyst at Perceptive Advisors, LLC, which is the investment manager of Perceptive Life Sciences Master Fund, Ltd. Dr. Hukkelhoven

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- owns an interest in Perceptive Life Sciences Master Fund, Ltd. but does not have voting or investment control over the shares held by Perceptive Life Sciences Master Fund, Ltd. and disclaims beneficial ownership over these shares, except to the extent of her pecuniary interest therein. The address of Perceptive Life Sciences Master Fund, Ltd. is c/o Perceptive Advisors LLC, 51 Astor Place, 10th Floor, New York, New York 10003.
- (3) Consists of 6,805,556 ordinary shares. The address of Adena Estate, Inc. is Craigmuir Chambers, P.O. Box 71, Road Town, Tortola, VG1110, British Virgin Islands.
  - (4) Consists of 5,501,309 ordinary shares and a warrant to purchase 900,000 ordinary shares. The address for Alexandria Equities No. 7, LLC is 385 E. Colorado Blvd., Suite 299, Pasadena, California 91101. One of our directors, Joel S. Marcus, is the Executive Chairman of ARE-QRS Corp., the general partner of Alexandria Real Estate Equities L.P., which is the managing member of ARE-Special Services, LLC, which is the managing member of Alexandria Equities No. 7, LLC.
  - (5) Consists of 4,246,808 ordinary shares.
  - (6) Consists of options to purchase 50,000 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.
  - (7) Consists of 3,320,871 ordinary shares and options to purchase 132,188 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.
  - (8) Consists of options to purchase 25,000 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.
  - (9) Consists of 5,501,309 ordinary shares and a warrant to purchase 900,000 ordinary shares held by Alexandria Equities No. 7, LLC, 310,180 ordinary shares held by Third Amended and Restated Joel and Barbara Marcus Family Trust and options held by Joel S. Marcus to purchase 50,000 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018. Joel Marcus, one of our directors, is the Executive Chairman of ARE-QRS Corp., the general partner of Alexandria Real Estate Equities L.P., which is the managing member of ARE-Special Services, LLC, which is the managing member of Alexandria Equities No. 7, LLC. ARE-QRS Corp. has full voting and investment power with respect to the shares owned by Alexandria Equities No. 7, LLC. As Executive Chairman of ARE-QRS Corp., Mr. Marcus may be deemed to have voting and investment power with respect to the shares owned by Alexandria Equities No. 7, LLC. Mr. Marcus disclaims beneficial ownership of the shares held by Alexandria Equities No. 7, LLC, except to the extent of his underlying pecuniary interest therein.
  - (10) Consists of 50,000 ordinary shares and options to purchase 50,000 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.
  - (11) Consists of 13,718,200 ordinary shares held by Kadmon Corporation, LLC, and 160,230 ordinary shares held by Gregory Moss. Gregory Moss, one of our directors, is Senior Vice President, Deputy Legal Counsel at Kadmon Holdings Inc., which is the sole member of Kadmon Corporation, LLC. Mr. Moss may be deemed to have voting and investment power with respect to the shares owned by Kadmon Corporation, LLC. Mr. Moss disclaims beneficial ownership of the shares held by Kadmon Corporation, LLC, except to the extent of his underlying pecuniary interest therein.
  - (12) Consists of 1,982,807 ordinary shares and options to purchase 56,250 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.
  - (13) Consists of 662,910 ordinary shares held by Double Epiphany, LLC and options held by Thomas Shenk to purchase 75,000 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018. The managing members of Double Epiphany, LLC are Thomas E. Shenk and Lillian W. Chiang, who have full voting and investment power with respect to the shares held by Double Epiphany, LLC. The address for Double Epiphany, LLC is 12 Boudinot Street, Princeton, New Jersey 08540.
  - (14) Consists of 2,219,271 ordinary shares and options to purchase 106,875 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.

## DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

*The following describes the issued share capital of MeiraGTx Holdings plc (the “Issuer”), summarizes the material provisions of the articles of association of the Issuer as are anticipated to be in effect upon the completion of this offering and highlights certain differences in corporate law in the Cayman Islands and Delaware, the United States. In this “Description of Share Capital and Articles of Association” discussion, we use the term “we,” “us” and “our” to refer to the Issuer.*

### General

We were incorporated pursuant to the laws of the Cayman Islands as an exempted company with limited liability to become the holding company of our business. Pursuant to the terms of our corporate reorganization, which will be completed prior to the completion of this offering, all of the issued share capital in MeiraGTx Limited will be exchanged for shares in the Issuer and, as a result, MeiraGTx Limited will become a wholly owned subsidiary of the Issuer. See “Corporate Reorganization” for more information.

The principal legislation under which the Issuer will operate and its shares will be issued is the Cayman Islands Companies Law (2018 Revision) (the “Companies Law”).

Our register of shareholders will be maintained by Computershare Trust Company N.A.

Following our corporate reorganization, certain resolutions will be required to be passed by our shareholders prior to the completion of this offering. These will include resolutions for the:

- adoption of new articles of association that will become effective upon the completion of this offering; and
- reorganization of the share capital of the Issuer.

### Share Capital

Upon completion of the Reorganization Transactions, our authorized share capital will consist of \$ divided into shares, par value \$ per share. Upon completion of the Reorganization Transactions and this offering, there will be ordinary shares issued and outstanding.

### Ordinary Shares

#### General

All of our issued and outstanding ordinary shares are fully paid and non assessable. Certificates representing our issued and outstanding ordinary shares are generally not issued and legal title to our issued shares is recorded in registered form in the register of members. Holders of our ordinary shares have no preemptive, subscription, redemption or conversion rights.

Our board of directors may provide for other classes of shares, including classes of preferred shares, out of our authorized but unissued share capital, which could be utilized for a variety of corporate purposes, including future offerings to raise capital for corporate purposes or for use in employee benefit plans. Such additional classes of shares shall have such rights, restrictions, preferences, privileges and payment obligations as determined by our board of directors. If we issue any preferred shares, the rights, preferences and privileges of holders of our ordinary shares will be subject to, and may be adversely affected by, the rights of the holders of such preferred shares. See “—Variation of rights.”

## **Dividends**

The holders of our ordinary shares are entitled to such dividends as may be declared by our board of directors subject to the Companies Law and our amended and restated memorandum and articles of association. Dividends and other distributions on issued and outstanding ordinary shares may be paid out of the funds of the Issuer lawfully available for such purpose, subject to any preference of any outstanding preferred shares. Dividends and other distributions will be distributed among the holders of our ordinary shares on a pro rata basis.

## ***Voting rights***

Voting at any shareholders' meeting is by show of hands, unless voting by way of poll demanded by the chairman of the board of directors or any shareholder present or voting by proxy. On a show of hands every shareholder present in person or by proxy shall have one vote and on a poll every shareholder present in person or by proxy shall have one vote for each ordinary share on all matters upon which the ordinary shares are entitled to vote.

A quorum required for a meeting of shareholders consists of holders with at least one-third of the votes eligible to be cast at any such general meeting of the Issuer.

An ordinary resolution to be passed by the shareholders requires the affirmative vote of a simple majority of the votes attaching to the ordinary shares cast in a general meeting, while a special resolution requires the affirmative vote of not less than two thirds of the votes attaching to the ordinary shares cast in a general meeting. An ordinary resolution or a special resolution may also be adopted by way of unanimous written resolution signed by or on behalf of each shareholder who would have been entitled to vote on such matter at a general meeting without a meeting being held. A special resolution will be required for matters such as certain merger or consolidation transactions, the change of name of the Issuer, making changes to our amended and restated memorandum and articles of association, or the voluntary winding up of the Issuer.

## ***Variation of rights***

The rights attached to any class of shares (unless otherwise provided by the terms of issue of that class), such as voting, dividends and the like, may be varied only with the sanction of a resolution passed by not less than two-thirds of the votes attaching to the shares of the relevant class cast in a meeting of the holders of the shares of that class, or by the written consent of the holders of not less than two-thirds of the shares of that class. The rights conferred upon the holders of the shares of any class shall not (unless otherwise provided by the terms of issue of that class) be deemed to be varied by the creation or issue of further shares ranking in priority to or *pari passu* with such previously existing shares.

## ***Transfer of ordinary shares***

Any of our shareholders may transfer all or any of his or her ordinary shares by an instrument of transfer in the usual or common form or any other form approved by our board of directors, subject to the applicable restrictions of our amended and restated memorandum and articles of association which will become effective upon the completion of this offering, such as the suspension of transfers for a period immediately preceding a general meeting, or the determination that a proposed transfer is not eligible.

## ***Liquidation***

On a return of capital on winding up or otherwise (other than on conversion, redemption or purchase of ordinary shares), assets available for distribution among the holders of ordinary shares shall be distributed among the holders of the ordinary shares on a pro rata basis.

### ***Directors***

The management of our company is vested in a board of directors. The quorum necessary for any meeting of our board of directors shall consist of at least a majority of the members of our board of directors and questions arising at any meeting shall be decided by a majority of votes.

Our amended and restated memorandum and articles of association, which will become effective upon completion of this offering, provide that our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of shareholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. The election of directors shall be by a plurality of the votes of the shares entitled to vote on the election of directors.

In addition, subject to the maximum number of directors designated by resolution of the board of directors, additional directors may be appointed from time to time by the board of Directors or by ordinary resolution either as a result of a casual vacancy or as an additional director.

Directors may be removed or replaced by an ordinary resolution of the shareholders.

### ***Indemnity of directors and officers***

Our amended and restated memorandum and articles of association provide that our board of directors and officers shall be indemnified from and against all liability which they incur in execution of their duty in their respective offices, except liability incurred by reason of such director's or officer's dishonesty, willful default or fraud.

### **Registration Rights**

Holders of Series C preferred shares, as of the effectiveness of Reorganization Transaction, who hold not less than 3% of the fully diluted share capital of the Company, and certain other holders will be entitled to certain rights with respect to the registration of ordinary shares for public resale under the Securities Act, pursuant to a Shareholder Agreement by and among us and certain of our shareholders. These rights terminate upon the earlier to occur of a deemed liquidation event, such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of a holder's shares without limitation during a three-month period without registration, and the third anniversary of our initial public offering. The registration of ordinary shares as a result of these rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

Subject to certain exceptions, including this offering, if we propose to register any of our ordinary shares in connection with a public offering of such securities solely for cash, we are obligated to notify the eligible holders of such registration. Upon the request of any such eligible holders given within 20 days following the registration notice, we are obligated, subject to certain exceptions, to register all of the ordinary shares then owned by the eligible holder that such holder has requested to be included in such registration. If the holders requesting registration intend to distribute their shares by means of an underwriting, the underwriters of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

### **Differences in Corporate Law**

Cayman Islands companies are governed by the Companies Law. The Companies Law is modeled on English law but does not follow recent English Law statutory enactments, and differs from laws applicable to United States corporations and their shareholders. Set forth below is a summary of some significant differences between the provisions of the Companies Law applicable to us and, for comparison purposes, the laws applicable to companies incorporated in the State of Delaware and their shareholders.

### ***Mergers and similar arrangements***

The Companies Law allows for the merger of two or more companies into either one consolidated company or one or more company(ies) merged into another so as to form a single surviving company. The merger or consolidation of two or more companies under Cayman Islands law requires the directors of the companies to enter into and to approve a written plan of merger or consolidation, which must also be authorized by a special resolution of each constituent company, in which regard see “— Ordinary Shares — Voting Rights” above, and such other authorization, if any, as may be specified in such companies’ articles of association. In relation to any merger or consolidation under the Companies Law, dissenting shareholders have certain limited appraisal rights in circumstances which are similar to those available to dissenting shareholders of a Delaware corporation, providing rights to receive payment in cash for the judicially determined fair value of the shares. Appraisal rights are ordinarily available where the consideration offered under the merger is payable in cash or, in some instances, the unlisted securities of a third party.

The Companies Law also includes statutory provisions that facilitate the reconstruction and amalgamation of companies, provided that such a scheme of arrangement is approved by shareholders or creditors who represent a majority in number and 75% in value of each such class of shareholders or creditors who attend and vote, either in person or by proxy, at a meeting or meetings convened for that purpose. The convening of meetings to consider any such scheme of arrangement, and the implementation of the scheme, must be sanctioned by the Grand Court of the Cayman Islands. While a dissenting shareholder has the right to express to the court the view that the transaction ought not to be approved, the court can be expected to approve the arrangement if it determines that:

- the statutory provisions as to the dual majority vote have been met;
- the shareholders have been fairly represented at the meeting in question and the classes properly delineated;
- the arrangement is such that a businessman would reasonably approve; and
- the arrangement is not one that would more properly be sanctioned under some other provision of the Companies Law.

If a scheme of arrangement is thus approved, the dissenting shareholders would have no rights comparable to appraisal rights, which would otherwise ordinarily be available to dissenting shareholders of a Delaware corporation.

When a tender offer to acquire shares is made and accepted (within four months) by holders of not less than 90% of the shares subject to such offer, the offeror may, within a two-month period following the expiration of the initial four month period, require the holders of the remaining shares to transfer such shares on the terms of the offer. An objection can be made to the Grand Court of the Cayman Islands but this is unlikely to succeed unless there is evidence of fraud, bad faith, collusion or inequitable treatment of shareholders.

### ***Shareholders’ suits***

We are not aware of any reported class action having been brought in a Cayman Islands court. Derivative actions have been brought in the Cayman Islands courts, and the Cayman Islands courts have confirmed the availability for such actions. In principle, we will normally be the proper plaintiff and a derivative action may not be brought by a shareholder. However, based on English authorities, which would in all likelihood be of persuasive authority in the Cayman Islands, there are exceptions to the foregoing principle, including when:

- a company acts or proposes to act illegally or ultra vires (beyond the scope of its authority);
- the act complained of, although not ultra vires, could be effected if duly authorized by a special resolution that has not been obtained; and

- those who control the company are perpetrating a “fraud on the minority.”

### ***Fiduciary duties of directors***

Under Delaware corporate law, a director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components, the duty of care and the duty of loyalty. The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director must act in a manner he or she reasonably believes to be in the best interests of the corporation. A director must not use his or her corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interests of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Should such evidence be presented concerning a transaction by a director, the director must prove the procedural fairness of the transaction and that the transaction was of fair value to the corporation.

As a matter of Cayman Islands law, a director of a Cayman Islands company is in the position of a fiduciary with respect to the company and therefore it is considered that he owes the following duties to the company: a duty to act in good faith and in what he considers to be in the best interests of the company; a duty not to make a profit out of his position as director (unless the company permits him to do so); a duty to exercise his powers for the purposes for which they are conferred; and a duty not to put himself in a position where the interests of the company conflict with his personal interest or his duty to a third party. A director of a Cayman Islands company owes to the company a duty to act with skill and care. A director will need to exhibit in the performance of his duties both the degree of skill than may reasonably be expected from a subjective perspective determined by reference to his knowledge and experience and the skill and care objectively to be expected from a person occupying office as a director of the company.

Under our amended and restated memorandum and articles of association, directors who are in any way, whether directly or indirectly, interested in a contract or proposed contract with our company must declare the nature of their interest at a meeting of the board of directors. Following such declaration, a director may vote in respect of any contract or proposed contract notwithstanding his interest; provided that, in exercising any such vote, such director’s duties remain as described above.

### ***Written consent of shareholders***

Under Delaware corporate law, unless otherwise provided in the certificate of incorporation, any action to be taken at any annual or special meeting of shareholders of a corporation may be taken by written consent of the holders of outstanding stock having not less than the minimum number of votes that would be necessary to take that action at a meeting at which all shareholders entitled to vote were present and voted. In addition, a corporation may eliminate the right of shareholders to act by written consent through amendment to its certificate of incorporation.

Cayman Islands law and our amended and restated memorandum and articles of association provide that shareholders may adopt an ordinary resolution or a special resolution by way of unanimous written resolution signed by or on behalf of each shareholder who would have been entitled to vote on such matter at a general meeting without a meeting being held.

### ***Shareholder proposals***

Under Delaware corporate law, a shareholder has the right to put any proposal before the shareholders at the annual meeting, provided that such shareholder complies with the notice provisions in the governing

documents. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings.

Under the laws of the Cayman Islands, a shareholder can only put a proposal before the shareholders at any general meeting in respect of any matter requiring a special resolution if it is set out in the notice calling the meeting. There is no right to introduce new business in respect of any matter requiring a special resolution at any meeting. A general meeting may be called by the board of directors or any other person authorized to do so in the articles of association, but shareholders may be precluded from calling general meetings. Under our amended and restated memorandum and articles of association general meetings shall also be convened on the requisition in writing of any shareholder or shareholders entitled to attend and vote at general meetings of the company and to exercise at least a majority of the voting power permitted to be exercised at any such meeting, deposited at the office specifying the objects of the meeting for a date no later than 21 days from the date of deposit of the requisition signed by such shareholders, and if the directors do not convene such meeting for a date not later than 45 days after the date of such deposit, such shareholders themselves may convene the general meeting in the same manner, as nearly as possible, as that in which general meetings may be convened by the directors, and all reasonable expenses incurred by such shareholders as a result of the failure of the directors to convene the general meeting shall be reimbursed to them by the company. As an exempted Cayman Islands company, we are not obliged by law to call shareholders' annual general meetings.

Under Delaware corporate law, a corporation is required to set a minimum quorum of one-third of the issued and outstanding shares for a shareholders meeting. Cayman Islands law permits a company's articles to have any quorum. See "— Ordinary Shares — Voting Rights."

#### ***Cumulative voting***

Under Delaware corporate law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation specifically provides for it. Cumulative voting potentially facilitates the representation of minority shareholders on a board of directors since it permits a minority shareholder to cast all the votes to which such shareholder is entitled on a single director, which increases such shareholder's voting power with respect to electing such director.

There are no prohibitions in relation to cumulative voting under the laws of the Cayman Islands, but our amended and restated memorandum and articles of association do not provide for cumulative voting. As a result, our shareholders are not afforded any less protection or fewer rights on this issue than shareholders of a Delaware corporation.

#### ***Election and removal of directors***

Under Delaware corporate law, unless otherwise specified in the certificate of incorporation or bylaws of a corporation, directors are elected by a plurality of the votes of the shares entitled to vote on the election of directors and may be removed with or without cause (or, with respect to a classified board, only with cause unless the certificate of incorporation provides otherwise) by the approval of a majority of the outstanding shares entitled to vote.

Similarly, as permitted by the Companies Law and pursuant to our amended and restated memorandum and articles of association, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of shareholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. The election of directors shall be by a plurality of the votes of the shares entitled to vote on the election of directors.

In addition, subject to the maximum number of directors designated by resolution of the board of directors, additional directors may be appointed from time to time by the board of Directors or by ordinary resolution either as a result of a casual vacancy or as an additional director.



Directors may be removed or replaced by an ordinary resolution of the shareholders.

***Written consent of directors***

Under Delaware corporate law, a written consent of the directors must be unanimous to take effect. The position under our amended and restated memorandum and articles of association is the same in this regard.

***Indemnification of directors and executive officers and limitation of liability***

Cayman Islands law does not limit the extent to which a company's amended and restated memorandum and articles of association may provide for indemnification of officers and directors, except to the extent any such provision may be held by the Cayman Islands courts to be contrary to public policy, such as to provide indemnification against civil fraud or the consequences of committing a crime. Our amended and restated memorandum and articles of association, which will become effective upon the completion of this offering, provide that our board of directors and officers shall be indemnified from and against all liability which they incur in execution of their duty in their respective offices, except liability incurred by reason of such directors' or officers' dishonesty, willful default or fraud. This standard of conduct is generally the same as permitted under Delaware corporate law.

***Enforcement of civil liabilities***

The Cayman Islands has a less developed body of securities laws as compared to the United States and provides less protection to investors. Additionally, Cayman Islands companies may not have standing to sue before the Federal courts of the United States. Although there is no statutory enforcement in the Cayman Islands of judgments obtained in the United States, the courts of the Cayman Islands will recognize a foreign judgment as the basis for a claim at common law in the Cayman Islands provided such judgment:

- is one in respect of which the foreign court had jurisdiction over the defendant according to Cayman Islands conflict of law rules;
- is final and conclusive;
- is either for a liquidated sum not in respect of penalties or taxes or a fine or similar fiscal or revenue obligations or, in certain circumstances, for *in personam* non-money relief; and
- was neither obtained in a manner, nor is of a kind enforcement of which is contrary to natural justice or the public policy of the Cayman Islands.

As a result of English case law, which will likely be highly persuasive in the Cayman Islands, the Cayman Islands Courts may also have discretion to enforce judgments obtained in foreign bankruptcy proceedings in other circumstances.

***Anti-money laundering — Cayman Islands***

In order to comply with legislation or regulations aimed at the prevention of money laundering, we are required to adopt and maintain anti-money laundering procedures, and may require subscribers to provide evidence to verify their identity and source of funds. Where permitted, and subject to certain conditions, we may also delegate the maintenance of our anti-money laundering procedures (including the acquisition of due diligence information) to a suitable person.

We reserve the right to request such information as is necessary to verify the identity of a subscriber. In the event of delay or failure on the part of the subscriber in producing any information required for verification purposes, we may refuse to accept the application, in which case any funds received will be returned without interest to the account from which they were originally debited.

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We also reserve the right to refuse to make any distribution payment to a shareholder if our directors or officers suspect or are advised that the payment of such distribution to such shareholder might result in a breach of applicable anti-money laundering or other laws or regulations by any person in any relevant jurisdiction, or if such refusal is considered necessary or appropriate to ensure our compliance with any such laws or regulations in any applicable jurisdiction.

If any person resident in the Cayman Islands knows or suspects or has reason for knowing or suspecting that another person is engaged in criminal conduct or is involved with terrorism or terrorist property and the information for that knowledge or suspicion came to their attention in the course of their business in the regulated sector, or other trade, profession, business or employment, the person will be required to report such knowledge or suspicion to (i) the Financial Reporting Authority of the Cayman Islands, pursuant to the Proceeds of Crime Law, 2017 (Law 10 of 2017) if the disclosure relates to criminal conduct or (ii) to a police officer of the rank of constable or higher, or the Financial Reporting Authority, pursuant to the Terrorism Law (2017 Revision) if the disclosure relates to involvement with terrorism or terrorist financing and property. Such a report shall not be treated as a breach of confidence or of any restriction upon the disclosure of information imposed by any enactment or otherwise.

### ***Variation of rights of shares***

Under Delaware corporate law, a corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise.

Under Cayman Islands law and our amended and restated memorandum and articles of association, if our share capital is divided into more than one class of shares, we may vary the rights attached to any class with the sanction of a resolution passed by not less than two-thirds of the votes attaching to the shares of the relevant class cast in a meeting of the holders of the shares of that class, or by the written consent of the holders of not less than two-thirds of the shares of that class.

### ***Sale of assets***

Under Delaware corporate law, a vote of the shareholders is required to approve a sale of assets only when all or substantially all assets are being sold to a person other than a subsidiary of the company.

The Companies Law contains no specific restrictions on the powers of directors to dispose of assets of a company. As a matter of general law, in the exercise of those powers, the directors must discharge their duties of care and to act in good faith, for a proper purpose and in the interests of the company.

### ***Transactions with interested shareholders***

The Delaware General Corporation Law contains a business combination statute applicable to Delaware corporations whereby, unless the corporation has specifically elected not to be governed by such statute by amendment to its certificate of incorporation, it is prohibited from engaging in certain business combinations with an "interested shareholder" for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or a group who or which owns or owned 15% or more of the target's outstanding voting stock within the past three years.

This has the effect of limiting the ability of a potential acquirer to make a two-tiered bid for the target in which all shareholders would not be treated equally. The statute does not apply if, among other things, prior to the date on which such shareholder becomes an interested shareholder, the board of directors approves either the business combination or the transaction which resulted in the person becoming an interested shareholder. This encourages any potential acquirer of a Delaware corporation to negotiate the terms of any acquisition transaction with the target's board of directors.

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Cayman Islands law has no comparable statute. As a result, we cannot avail ourselves of the types of protections afforded by the Delaware business combination statute. However, although Cayman Islands law does not regulate transactions between a company and its significant shareholders, it does provide that such transactions must be entered into bona fide in the best interests of the company and not with the effect of constituting a fraud on the minority shareholders.

### ***Rights of non-resident or foreign shareholders***

There are no limitations imposed by our amended and restated memorandum and articles of association on the rights of non-resident or foreign shareholders to hold or exercise voting rights on our shares. As similarly provided under Delaware corporate law, there are no restrictions on foreign or non-resident ownership or management of a Cayman Islands exempted company under Cayman Islands law. In addition, there are no provisions in our amended and restated memorandum and articles of association governing the ownership threshold above which shareholder ownership must be disclosed.

### ***Dissolution and winding up***

Under the Delaware General Corporation Law, unless the board of directors approves the proposal to dissolve, dissolution must be approved by shareholders holding 100% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with a dissolution initiated by the board of directors. Under the Companies Law of the Cayman Islands and our amended and restated memorandum and articles of association, our company may be voluntarily dissolved, liquidated or wound up only by a special resolution of our shareholders, in which regard see “— Ordinary Shares — Voting Rights” above. In addition, a company may be wound up by the Grand Court of the Cayman Islands if the company is unable to pay its debts or if the court is of the opinion that it is just and equitable that our company is wound up.

### ***Inspection of books and records***

Under Delaware corporate law, any shareholder of a corporation may for any proper purpose inspect or make copies of the corporation's stock ledger, list of shareholders and other books and records.

Our shareholders will have no general right under Cayman Islands law to inspect or obtain copies of our list of shareholders or corporate records except our memorandum and restated articles of association.

### ***Amendment of governing documents***

Under Delaware corporate law, a corporation's certificate of incorporation may be amended only if adopted and declared advisable by the board of directors and approved by a majority of the outstanding shares entitled to vote, and the bylaws may be amended with the approval of a majority of the outstanding shares entitled to vote and may, if so provided in the certificate of incorporation, also be amended by the board of directors. As permitted by Cayman Islands law, our amended and restated memorandum and articles of association may be amended with the sanction of a special resolution of shareholders.

### ***Transfer Agent and Registrar***

The transfer agent and registrar for our ordinary shares will be Computershare Trust Company, N.A.

### ***Stock Exchange Listing***

We applied to have our ordinary shares listed on the Nasdaq Global Market under the symbol “MGTX.”

## SHARES ELIGIBLE FOR FUTURE SALE

Immediately prior to this offering, there was no public market for our ordinary shares. Future sales of substantial amounts of ordinary shares in the public market, or the perception that such sales may occur, could adversely affect the market price of our ordinary shares.

Upon the closing of this offering, we will have outstanding an aggregate of \_\_\_\_\_ ordinary shares, assuming the issuance of \_\_\_\_\_ ordinary shares offered by us in this offering (or \_\_\_\_\_ ordinary shares if the underwriters exercise their option to purchase additional shares in full), and no exercise of options after \_\_\_\_\_, 2018. Of these shares, all shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our “affiliates,” as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining \_\_\_\_\_ ordinary shares will be “restricted securities,” as that term is defined in Rule 144 under the Securities Act. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below. We expect that substantially all of these shares will be subject to the 180-day lock-up period under the lock-up agreements described below. Upon expiration of the lock-up period, we estimate that approximately \_\_\_\_\_ shares will be available for sale in the public market, subject in some cases to applicable volume limitations under Rule 144.

In addition, of the \_\_\_\_\_ ordinary shares that were subject to share options outstanding as of \_\_\_\_\_, 2018, options to purchase \_\_\_\_\_ ordinary shares were vested as of \_\_\_\_\_, 2018 and, upon exercise, these shares will be eligible for sale subject to the lock-up agreements described below and Rules 144 and 701 under the Securities Act.

### Lock-up Agreements

We and each of our directors and executive officers and holders of substantially all of our outstanding ordinary shares have agreed that, without the prior written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Barclays Capital Inc., we and they will not, subject to certain exceptions, during the period ending 180 days after the date of this prospectus, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any ordinary shares or any securities convertible into or exercisable or exchangeable for ordinary shares; or enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our ordinary shares, whether any transaction described above is to be settled by delivery of our ordinary shares or such other securities, in cash or otherwise.

Upon the expiration of the lock-up period, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above. For a further description of these lock-up agreements, please see “Underwriting.”

### Rule 144

#### *Affiliate Resales of Restricted Securities*

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned ordinary shares for at least six months would be entitled to sell in

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“broker’s transactions” or certain “riskless principal transactions” or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of ordinary shares then outstanding, which will equal approximately \_\_\_\_\_ shares immediately after the closing of this offering based on the number of ordinary shares outstanding as of \_\_\_\_\_ ; or
- the average weekly trading volume in our ordinary shares on the Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Such sales by affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

### ***Non-Affiliate Resales of Restricted Securities***

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the 90 days preceding a sale, and who has beneficially owned ordinary shares for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

### **Rule 701**

In general, under Rule 701, any of an issuer’s employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a compensatory stock or option plan, or other written agreements, before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

The Securities and Exchange Commission has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

### **Equity Plans**

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all ordinary shares subject to outstanding stock options and ordinary shares issued or issuable under our stock plans. We expect to file the registration statement covering shares offered pursuant to our stock plans shortly after the date of this prospectus, permitting the resale of such shares by non-affiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144.

## **MATERIAL CAYMAN ISLANDS TAX CONSIDERATIONS**

The following discussion is a summary of the material Cayman Islands tax considerations relating to the purchase, ownership and disposition of our ordinary shares. There is, at present, no direct taxation in the Cayman Islands and interest, dividends and gains payable to the company will be received free of all Cayman Islands taxes. The company has received an undertaking from the Government of the Cayman Islands to the effect that, for a period of twenty years from the date of the undertaking, no law that thereafter is enacted in the Cayman Islands imposing any tax or duty to be levied on profits, income or on gains or appreciation, or any tax in the nature of estate duty or inheritance tax, will apply to any property comprised in or any income arising under the company, or to the shareholders thereof, in respect of any such property or income.

No stamp duty in the Cayman Islands is payable in respect of the issue of any ordinary shares or an instrument of transfer in respect of an ordinary share.

## CERTAIN UNITED KINGDOM TAX CONSIDERATIONS

The following statements are of a general nature and do not purport to be a complete analysis of all potential UK tax consequences of acquiring, holding and disposing of our ordinary shares. They are based on current UK tax law and on the current published practice of Her Majesty's Revenue and Customs ("HMRC") (which may not be binding on HMRC), as of the date of this prospectus, all of which are subject to change, possibly with retrospective effect. They are intended to address only certain United Kingdom tax consequences for holders of our ordinary shares who are tax resident in (and only in) the United Kingdom, and in the case of individuals, domiciled in (and only in) the United Kingdom (except where expressly stated otherwise) who are the absolute beneficial owners of our ordinary shares and any dividends paid on them and who hold our ordinary shares as investments (other than in an individual savings account or a self-invested personal pension). They do not address the UK tax consequences which may be relevant to certain classes of holders of our ordinary shares such as traders, brokers, dealers, banks, financial institutions, insurance companies, investment companies, collective investment schemes, tax-exempt organizations, trustees, persons connected with us or a member of our group, persons holding our ordinary shares as part of hedging or conversion transactions, holders of our ordinary shares who have (or are deemed to have) acquired our ordinary shares by virtue of an office or employment, and holders of our ordinary shares who are or have been officers or employees of us or a company forming part of our group. The statements do not apply to any holder of our ordinary shares who either directly or indirectly holds or controls 10% or more of the our share capital (or class thereof), voting power or profits.

The following is intended only as a general guide and is not intended to be, nor should it be considered to be, legal or tax advice to any particular prospective subscriber for, or purchaser of, our ordinary shares. Accordingly, prospective subscribers for, or purchasers of, our ordinary shares who are in any doubt as to their tax position regarding the acquisition, ownership and disposition of our ordinary shares or who are subject to tax in a jurisdiction other than the United Kingdom should consult their own tax advisers.

### **The Company**

It is the intention of the directors to conduct the affairs of the Company so that the central management and control of the Company is exercised in the UK. As a result, the Company is expected to be treated as resident in the UK for UK tax purposes. Accordingly we expect to be subject to UK taxation on our income and gains, except where an exemption applies.

We may be treated as a dual resident company for UK tax purposes. As a result, our right to claim certain reliefs from UK tax may be restricted, and changes in law or practice in the United Kingdom could result in the imposition of further restrictions on our right to claim UK tax reliefs.

### **Taxation of dividends**

#### ***Withholding tax***

We will not be required to withhold UK tax at source when paying dividends on our ordinary shares.

#### ***Income tax***

An individual holder of our ordinary shares who is resident for tax purposes in the UK may, depending on his or her particular circumstances, be subject to UK tax on dividends received from us. Dividend income is treated as the top slice of the total income chargeable to UK income tax. An individual holder of our ordinary shares who is not resident for tax purposes in the UK should not be chargeable to UK income tax on dividends received from us unless he or she carries on (whether solely or in partnership) any trade, profession or vocation in the UK through a permanent establishment to which our ordinary shares are attributable. There are certain exceptions for trading in the UK through independent agents, such as some brokers and investment managers.

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All dividends received by a UK resident individual holder of our ordinary shares from us or from other sources will form part of that holder's total income for income tax purposes and will constitute the top slice of that income. A nil rate of income tax will apply to the first £2,000 of taxable dividend income received by the holder of our ordinary shares in a tax year. Income within the nil rate band will be taken into account in determining whether income in excess of the nil rate band falls within the basic rate, higher rate or additional rate tax bands. Where the dividend income is above the £2,000 dividend allowance, the first £2,000 of the dividend income will be charged at the nil rate and any excess amount will be taxed at 7.5 per cent. to the extent that the excess amount falls within the basic rate tax band, 32.5 per cent. to the extent that the excess amount falls within the higher rate tax band and 38.1 per cent. to the extent that the excess amount falls within the additional rate tax band.

### **Corporation tax**

Corporate holders of our ordinary shares which are resident for tax purposes in the UK should not be subject to UK corporation tax on any dividend received from us so long as the dividends qualify for exemption (as is likely) and certain conditions are met (including anti-avoidance conditions). Corporate holders of our ordinary shares which are not resident in the United Kingdom will not generally be subject to UK corporation tax on dividends unless they are carrying on a trade, profession or vocation in the United Kingdom through a permanent establishment in connection with which such shares are attributable.

A holder of our ordinary shares who is resident outside the United Kingdom may be subject to non-UK taxation on dividend income under local law.

### **Taxation of capital gains**

#### ***UK resident holders of our ordinary shares***

A disposal or deemed disposal of our ordinary shares by an individual or corporate holder of such shares who is tax resident in the United Kingdom may, depending on that holder's circumstances and subject to any available exemptions or reliefs, give rise to a chargeable gain or allowable loss for the purposes of UK taxation of chargeable gains.

Any chargeable gain (or allowable loss) will generally be calculated by reference to the consideration received for the disposal of our ordinary shares less the allowable cost to the holder of acquiring such shares.

The applicable tax rates for individual holders of our ordinary shares realizing a gain on the disposal of such shares is, broadly, 10% for basic rate taxpayers and 20% for higher and additional rate taxpayers. The applicable tax rates for corporate holders of our ordinary shares realizing a gain on the disposal of such shares is currently 19%.

#### ***Non-UK holders of our ordinary shares***

Holders of our ordinary shares who are not resident in the United Kingdom and, in the case of an individual holder of our ordinary shares, not temporarily non-resident, should not be liable for UK tax on capital gains realized on a sale or other disposal of our ordinary shares unless such shares are attributable to a trade, profession or vocation carried on in the United Kingdom through a branch or agency or, in the case of a corporate holder of our ordinary shares, through a permanent establishment. Holders of our ordinary shares who are not resident in the United Kingdom may be subject to non-UK taxation on any gain under local law.

Generally, an individual holder of our ordinary shares who has ceased to be resident in the United Kingdom for tax purposes for a period of five years or less and who disposes of our ordinary shares during that period may be liable on their return to the United Kingdom to UK taxation on any capital gain realized (subject to any available exemption or relief).



## **UK stamp duty (“Stamp Duty”) and UK stamp duty reserve tax (“SDRT”)**

The statements below are intended as a general guide to the current position relating to Stamp Duty and SDRT and apply to any holders of our ordinary shares irrespective of their place of tax residence.

No UK Stamp Duty or SDRT, will be payable on the issue of ordinary shares, subject to the comments below.

Stamp Duty will in principle be payable on any instrument of transfer of ordinary shares that is executed in the United Kingdom or that relates to any property situated, or to any matter or thing done or to be done, in the United Kingdom. An exemption from Stamp Duty is available on an instrument transferring ordinary shares where the amount or value of the consideration is £1,000 or less and it is certified on the instrument that the transaction effected by the instrument does not form part of a larger transaction or series of transactions in respect of which the aggregate amount or value of the consideration exceeds £1,000. Holders of ordinary shares should be aware that, even where an instrument of transfer is in principle subject to Stamp Duty, Stamp Duty is not required to be paid unless it is necessary to rely on the instrument for legal purposes, for example to register a change of ownership or in litigation in a UK court.

Provided that ordinary shares are not registered in any register maintained in the United Kingdom by or on behalf of us and are not paired with any shares issued by a UK incorporated company, any agreement to transfer ordinary shares will not be subject to SDRT. The ordinary shares are not paired with any shares issued by a UK incorporated company and we currently do not intend that any register of ordinary shares will be maintained in the United Kingdom.

If ordinary shares were to be registered in a register maintained in the United Kingdom by or on behalf of us or paired with any shares issued by a UK incorporated company then, subject to the comments below, where ordinary shares are transferred or issued to, or to a nominee or agent for, a person whose business is or includes the provision of clearance services or issuing depositary receipts (but not including CREST), SDRT may be payable at a rate of 1.5% of the amount or value of the consideration payable for (or, in certain circumstances, the value of) the ordinary shares. This liability for SDRT will be payable by the clearance service or depositary receipt operator or its nominee, as the case may be, but in practice participants in the clearance service or depositary receipt scheme will generally be required to reimburse them for such cost. It is understood that H.M. Revenue and Customs regards the facilities of DTC as a clearance service for these purposes.

Following litigation, H.M. Revenue and Customs has confirmed that it will no longer seek to apply the above 1.5% SDRT charge (or a corresponding Stamp Duty charge) on the issue of shares into a clearance service or depositary receipt system established in a European Member State on the basis that the charge is not compatible with EU law. However, their view is that the 1.5% charge will still apply to the transfer of shares into such a clearance service or depositary receipts system where the transfer is not an integral part of the issue of share capital. There is an exception from the 1.5% charge on the transfer to, or to a nominee or agent for, a clearance service where the clearance service has made and maintained an election under section 97A(1) of the UK Finance Act 1986 which has been approved by HMRC. We are not aware of any section 97A election having been made by DTC. Accordingly, holders of ordinary shares should consult their own independent professional advisers before incurring or reimbursing the costs of such a 1.5% SDRT charge.

## MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES

The following discussion describes the material U.S. federal income tax consequences to U.S. Holders (as defined below) under present law of an investment in our ordinary shares. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire the ordinary shares. The effects of any applicable state or local laws, other U.S. federal tax laws such as estate and gift tax laws, the alternative minimum tax or the Medicare contribution tax on net investment income, are not discussed. This summary applies only to investors who acquire the ordinary shares in exchange for cash, hold the ordinary shares as capital assets (generally, property held for investment) and who have the U.S. dollar as their functional currency. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, U.S. Treasury regulations promulgated thereunder, judicial decisions, published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or the IRS, all as in effect as of the date of this prospectus. All of the foregoing authorities are subject to change, which change could apply retroactively and could alter the tax consequences described below.

The following discussion does not address all U.S. federal income tax consequences relevant to a holder's particular circumstances or to holders subject to particular rules, including:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons whose functional currency is not the U.S. dollar;
- persons holding ordinary shares as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers or traders in securities, commodities or currencies;
- S corporations or entities or arrangements treated as partnerships for U.S. federal income tax purposes;
- tax-exempt organizations or governmental organizations;
- individual retirement accounts or other tax deferred accounts;
- persons who acquired the ordinary shares pursuant to the exercise of any employee share option or otherwise as compensation;
- persons that own or are deemed to own 10% or more of our stock by vote or value;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to the ordinary shares being taken into account in an applicable financial statement;
- persons that hold ordinary shares through a permanent establishment or fixed base outside the United States; and
- persons deemed to sell ordinary shares under the constructive sale provisions of the Code.

**U.S. HOLDERS ARE URGED TO CONSULT THEIR TAX ADVISORS REGARDING THE APPLICATION OF THE U.S. FEDERAL TAX RULES TO THEIR PARTICULAR CIRCUMSTANCES AS WELL AS THE U.S. STATE, LOCAL AND NON-U.S. TAX CONSEQUENCES TO THEM OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF ORDINARY SHARES.**

For purposes of this discussion, a "U.S. Holder" is a beneficial owner of ordinary shares that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;

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- a corporation (or another entity taxable as a corporation) created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the supervision of a U.S. court and the control of one or more “United States persons” (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

If you are a partner in an entity taxable as a partnership for U.S. federal income tax purposes that holds ordinary shares, your tax treatment generally will depend on your status and the activities of the partnership. Partnerships holding ordinary shares and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences applicable to them.

### **Taxation of Dividends and Other Distributions on the Ordinary Shares**

The discussion in this section “Taxation of Dividends and Other Distributions on the Ordinary Shares” is subject to the discussion regarding passive foreign investment companies below.

As discussed above under “Dividend Policy,” the Company does not currently intend to declare dividends on the ordinary shares in the foreseeable future. In the event the Company does pay dividends, the gross amount of any distribution to you with respect to the ordinary shares will be included in your gross income as dividend income when actually or constructively received to the extent the distribution is paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). To the extent the amount of the distribution exceeds our current and accumulated earnings and profits, it will be treated first as a return of your tax basis in the ordinary shares, and to the extent the amount of the distribution exceeds your tax basis, the excess will be taxed as capital gain. We do not intend to calculate our earnings and profits under U.S. federal income tax principles. Therefore, a U.S. Holder should expect that distributions will generally be reported as ordinary dividend income for such purposes. Dividends we pay will not be eligible for the dividends-received deduction available to corporations in respect of dividends received from U.S. corporations.

Subject to certain limitations, dividends paid by qualified foreign corporations to certain non-corporate U.S. Holders may be taxable at preferential tax rates. A non-U.S. corporation is generally treated as a qualified foreign corporation with respect to dividends paid on stock that is readily tradable on a securities market in the United States, such as the NASDAQ Global Select Market, on which the Company has applied to list the ordinary shares. However, the preferential tax rates discussed above will not apply if we are treated as a passive foreign investment company with respect to the U.S. Holder for the taxable year in which a dividend is paid or the preceding year. Non-corporate U.S. Holders should consult their tax advisers regarding the availability of the reduced tax rate on dividends. Dividends will be included in a U.S. Holder’s income on the date of the U.S. Holder’s receipt of the dividend.

Dividends will generally constitute foreign source income for foreign tax credit limitation purposes. Any tax withheld with respect to distributions on the ordinary shares may, subject to a number of complex limitations, be claimed as a foreign tax credit against such U.S. Holder’s U.S. federal income tax liability or may be claimed as a deduction for U.S. federal income tax purposes. The limitation on foreign taxes eligible for credit is calculated separately with respect to specific classes of income. For this purpose, dividends distributed by us with respect to the ordinary shares generally will constitute “passive category income.” The rules with respect to the foreign tax credit are complex and may depend upon a U.S. Holder’s particular circumstances. You should consult your tax advisor regarding the availability of the foreign tax credit in light of your particular circumstances.

### **Taxation of Disposition of the Ordinary Shares**

The discussion in this section “Taxation of Disposition of the Ordinary Shares” is subject to the discussion regarding passive foreign investment companies below.

You will recognize gain or loss on any sale, exchange or other taxable disposition of ordinary shares equal to the difference between the amount realized (in U.S. dollars) on the disposition and your tax basis (in U.S. dollars) in the ordinary shares. Any such gain or loss will be capital gain or loss, and will be long-term capital gain or loss if you have held the ordinary shares for more than one year at the time of the disposition. Otherwise, such gain or loss will be short-term capital gain or loss. Long-term capital gains recognized by certain non-corporate U.S. Holders, including individuals, generally will be taxable at reduced rates. The deductibility of capital losses is subject to limitations. Any such gain or loss you recognize generally will be treated as U.S. source income or loss for foreign tax credit limitation purposes. You should consult your tax advisor regarding the proper treatment of gain or loss in your particular circumstances.

### **Passive Foreign Investment Company**

Based on the current and anticipated value of our assets and the composition of our income, assets and operations, we do not believe we were a “passive foreign investment company,” or PFIC, for the taxable year ending on December 31, 2017, and do not expect to be a PFIC for current taxable year. However, the application of the PFIC rules is subject to uncertainty in several respects, and we cannot assure you that the IRS will not take a contrary position. A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either:

- at least 75% of its gross income for such taxable year is passive income, or
- at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income.

For purposes of the above calculations, if a non-U.S. corporation owns, directly or indirectly, 25% or more of the total value of the outstanding shares of another corporation, it will be treated as if it (a) held a proportionate share of the assets of such other corporation and (b) received directly a proportionate share of the income of such other corporation. Passive income generally includes dividends, interest, rents, royalties and capital gains, but generally excludes rents and royalties which are derived in the active conduct of a trade or business and which are received from a person other than a related person.

A separate determination must be made each taxable year as to whether we are a PFIC (after the close of each such taxable year). Because the value of our assets for purposes of the asset test will generally be determined by reference to the market price of the ordinary shares, our PFIC status will depend in large part on the market price of the ordinary shares, which may fluctuate significantly. In addition, changes in the composition of our income or assets may cause us to become a PFIC.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns ordinary shares, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the ordinary shares, regardless of whether we continue to meet the tests described above unless we cease to be a PFIC and the U.S. Holder has made a “deemed sale” election under the PFIC rules.

If we are a PFIC for any taxable year during which you hold ordinary shares, you will be subject to special tax rules with respect to any “excess distribution” you receive and any gain you realize from a sale or other disposition (including a pledge) of ordinary shares. Distributions you receive in a taxable year that are greater than 125% of the average annual distributions you received during the shorter of the three preceding taxable years or your holding period for the ordinary shares will be treated as an excess distribution. Under these special tax rules, if you receive any excess distribution or realize any gain from a sale or other disposition of the ordinary shares:

- the excess distribution or gain will be allocated ratably over your holding period for the ordinary shares,

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- the amount allocated to the current taxable year, and any taxable year before the first taxable year in which we were a PFIC, will be treated as ordinary income, and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and an interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years before the year of disposition or “excess distribution” cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of ordinary shares cannot be treated as capital, even if you hold the ordinary shares as capital assets.

Certain elections may be available that would result in alternative treatments (such as mark-to-market treatment of the common shares). The adverse consequences of owning stock in a PFIC could be mitigated if a U.S. Holder makes a valid “qualified electing fund” election, or QEF election, which, among other things, would require a U.S. Holder to include currently in income its pro rata share of the PFIC’s net capital gain and ordinary earnings, based on earnings and profits as determined for U.S. federal income tax purposes. We have not yet determined whether we would provide the information necessary for U.S. Holders of our ordinary shares to make qualified electing fund elections in the event we are or were classified as a PFIC.

If we are considered a PFIC, U.S. Holders will also be subject to annual information reporting requirements. If we are or become a PFIC, you should consult your tax advisor regarding any reporting requirements that may apply to you. U.S. Holders are urged to consult their tax advisors regarding the application of the PFIC rules to the ownership and disposition of the ordinary shares and the potential availability of a mark-to-market or QEF election.

### **Information Reporting and Backup Withholding**

Dividend payments with respect to ordinary shares and proceeds from the sale, exchange or other disposition of ordinary shares may be subject to information reporting to the IRS and U.S. backup withholding. Certain U.S. Holders are exempt from backup withholding, including corporations and certain tax-exempt organizations. A U.S. Holder will be subject to backup withholding if such holder is not otherwise exempt and such holder:

- fails to furnish the holder’s taxpayer identification number, which for an individual is ordinarily his or her social security number;
- furnishes an incorrect taxpayer identification number;
- is notified by the IRS that the holder previously failed to properly report payments of interest or dividends; or
- fails to certify under penalties of perjury that the holder has furnished a correct taxpayer identification number and that the IRS has not notified the holder that the holder is subject to backup withholding.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against the U.S. Holder’s U.S. federal income tax liability, provided the required information is timely furnished to the IRS. U.S. Holders should consult their tax advisors regarding their qualification for an exemption from backup withholding and the procedures for obtaining such an exemption.

### **Additional Reporting Requirements**

Certain U.S. Holders who are individuals (and certain entities) that hold an interest in “specified foreign financial assets” (which may include the ordinary shares) are required to report information relating to such

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assets, subject to certain exceptions (including an exception for ordinary shares held in accounts maintained by certain financial institutions). Penalties can apply if U.S. Holders fail to satisfy such reporting requirements. U.S. Holders should consult their tax advisors regarding the applicability of these requirements to their acquisition and ownership of ordinary shares.

## UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated and Barclays Capital Inc. are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of ordinary shares set forth opposite its name below.

<u>Underwriter</u>	<u>Number of Ordinary Shares</u>
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Barclays Capital Inc.	
Evercore Group L.L.C.	
Chardan Capital Markets LLC	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the ordinary shares sold under the underwriting agreement if any of these ordinary shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the ordinary shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the ordinary shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

### Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the ordinary shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of \$ per ordinary share. After the initial offering, the public offering price, concession or any other term of the offering may be changed. We have also agreed to reimburse the underwriters for an aggregate of up to \$ for certain of their offering expenses, including counsel fees and expenses in connection with the clearance of this offering with the Financial Industry Regulatory Authority, or FINRA. In accordance with FINRA Rule 5110, these reimbursed expenses are deemed underwriting compensation for this offering.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional ordinary shares.

	<u>Per Ordinary Share</u>	<u>Without Option</u>	<u>With Option</u>
Public offering price	\$	\$	\$
Underwriting discount	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

MeiraGTx Holdings plc

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The expenses of the offering, not including the underwriting discount, are estimated at \$ \_\_\_\_\_ and are payable by us.

### **Option to Purchase Additional Ordinary Shares**

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to \_\_\_\_\_ additional ordinary shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional ordinary shares proportionate to that underwriter's initial amount reflected in the above table.

### **No Sales of Similar Securities**

We, our executive officers and directors and our other existing security holders have agreed not to sell or transfer any ordinary shares or securities convertible into, exchangeable for, exercisable for, or repayable with ordinary shares, for 180 days after the date of this prospectus without first obtaining the written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Barclays Capital Inc. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any ordinary shares,
- sell any option or contract to purchase any ordinary shares,
- purchase any option or contract to sell any ordinary shares,
- grant any option, right or warrant for the sale of any ordinary shares,
- lend or otherwise dispose of or transfer any ordinary shares,
- request or demand that we file a registration statement related to the ordinary shares, or
- enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any ordinary shares whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to ordinary shares and to securities convertible into or exchangeable or exercisable for or repayable with ordinary shares. It also applies to ordinary shares owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

### **Nasdaq Global Market Listing**

We expect the ordinary shares to be approved for listing on the Nasdaq Global Market, subject to notice of issuance, under the symbol "MGTX."

Before this offering, there has been no public market for our ordinary shares. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price will be:

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us,
- our financial information,



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- the history of, and the prospects for, our company and the industry in which we compete,
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues,
- the present state of our development, and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the ordinary shares may not develop. It is also possible that after the offering the ordinary shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the ordinary shares in the aggregate to accounts over which they exercise discretionary authority.

### **Price Stabilization, Short Positions and Penalty Bids**

Until the distribution of the ordinary shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our ordinary shares. However, the representatives may engage in transactions that stabilize the price of the ordinary shares, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our ordinary shares in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of ordinary shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional ordinary shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional ordinary shares or purchasing ordinary shares in the open market. In determining the source of ordinary shares to close out the covered short position, the underwriters will consider, among other things, the price of ordinary shares available for purchase in the open market as compared to the price at which they may purchase ordinary shares through the option granted to them. "Naked" short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing ordinary shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our ordinary shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of ordinary shares made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased ordinary shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our ordinary shares or preventing or retarding a decline in the market price of our ordinary shares. As a result, the price of our ordinary shares may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our ordinary shares. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

## **Electronic Distribution**

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

## **Other Relationships**

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

## **Notice to Prospective Investors in the European Economic Area**

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each referred to as a “Member State”), no offer of ordinary shares which are the subject of the offering has been, or will be, made to the public in that Member State, other than under the following exemptions under the Prospectus Directive, if they have been implemented in that Member State:

- (a) to any legal entity which is a “qualified investor” as defined in the Prospectus Directive;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the Underwriters for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

*provided* that no such offer of ordinary shares referred to in (a) to (c) above shall result in a requirement for the Company or any Underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive, or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person located in a Member State to whom any offer of ordinary shares is made or who receives any communication in respect of an offer of ordinary shares, or who initially acquires any ordinary shares, will be deemed to have represented, warranted, acknowledged and agreed to and with each Underwriter and the Company that (1) it is a “qualified investor” within the meaning of the law in that Member State implementing Article 2(1)(e) of the Prospectus Directive; and (2) in the case of any ordinary shares acquired by it as a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, the ordinary shares acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the Underwriters has been given to the offer or resale; or where ordinary shares have been acquired by it on behalf of persons in any Member State other than qualified investors, the offer of those ordinary shares to it is not treated under the Prospectus Directive as having been made to such persons.

The Company, the Underwriters and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgments and agreements.

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This document has been prepared on the basis that any offer of ordinary shares in any Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of ordinary shares. Accordingly any person making or intending to make an offer in that Member State of ordinary shares which are the subject of the offering contemplated in this document may only do so in circumstances in which no obligation arises for the Company or any of the Underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the Underwriters have authorized, nor do they authorize, the making of any offer of ordinary shares in circumstances in which an obligation arises for the Company or the Underwriters to publish a prospectus for such offer.

For the purposes of this provision, the expression an “offer of ordinary shares to the public” in relation to any ordinary shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe for the ordinary shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (as amended) and includes any relevant implementing measure in each Member State and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

The above selling restriction is in addition to any other selling restrictions set out below.

### **Notice to Prospective Investors in the United Kingdom**

In the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (e) of the Order (all such persons together being referred to as “relevant persons”).

Each of the underwriters has represented and agreed that:

- (a) it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended) (referred to as “FSMA”), except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the U.K. Financial Conduct Authority;
- (b) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to relevant persons; and
- (c) it has complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

This document and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Neither this document nor any of its contents must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

### **Notice to Prospective Investors in Switzerland**

The ordinary shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (“SIX”) or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the ordinary shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the ordinary shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of ordinary shares will not be supervised by, the Swiss Financial Market Supervisory Authority, or FINMA, and the offer of ordinary shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of ordinary shares.

### **Notice to Prospective Investors in the Dubai International Financial Centre**

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority (“DFSA”). This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The ordinary shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the ordinary shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

### **Notice to Prospective Investors in Australia**

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission (“ASIC”), in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the “Corporations Act”), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the “Exempt Investors”) who are “sophisticated investors” (within the meaning of section 708(8) of the Corporations Act), “professional investors” (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the ordinary shares without disclosure to investors under Chapter 6D of the Corporations Act.

The ordinary shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring ordinary shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities

recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

#### **Notice to Prospective Investors in Hong Kong**

The ordinary shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the ordinary shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to ordinary shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

#### **Notice to Prospective Investors in Japan**

The ordinary shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, “Japanese Person” shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

#### **Notice to Prospective Investors in Singapore**

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of ordinary shares may not be circulated or distributed, nor may the ordinary shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the “SFA”), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the ordinary shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

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securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the ordinary shares pursuant to an offer made under Section 275 of the SFA except:

- (a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- (b) where no consideration is or will be given for the transfer;
- (c) where the transfer is by operation of law;
- (d) as specified in Section 276(7) of the SFA; or
- (e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

### **Notice to Prospective Investors in Canada**

The ordinary shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the ordinary shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

## LEGAL MATTERS

The validity of our ordinary shares and certain other matters of Cayman Islands law will be passed upon for us by Walkers, 190 Elgin Avenue, George Town, Grand Cayman KY1-9001, Cayman Islands. Certain other matters will be passed upon for us by Latham & Watkins LLP. Certain legal matters in connection with this offering will be passed upon for the underwriters by Cooley LLP.

## EXPERTS

The consolidated financial statements of MeiraGTx Limited and Subsidiaries at December 31, 2017 and 2016, and for each of the two years in the period ended December 31, 2017, appearing in this Prospectus and Registration Statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements) appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

## ENFORCEMENT OF CIVIL LIABILITIES

We are incorporated under the laws of the Cayman Islands. We have been advised that there is some doubt as to the enforceability in the Cayman Islands, in original actions or in actions for enforcement of judgments of U.S. courts, of civil liabilities based solely on the federal securities laws of the United States. In addition, awards for punitive damages in actions brought in the United States or elsewhere may be unenforceable in the Cayman Islands. An award for monetary damages under the U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered and is intended to punish the defendant. The enforceability of any judgment in the Cayman Islands will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and the Cayman Islands do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

We have appointed MeiraGTx, LLC as our agent to receive service of process with respect to any action brought against us in the United States District Court for the Southern District of New York under the federal securities laws of the United States or of any state in the United States or any action brought against us in the Supreme Court of the State of New York in the County of New York under the securities laws of the State of New York.

We have been advised by our Cayman Islands legal counsel that the courts of the Cayman Islands are unlikely (i) to recognize or enforce against us judgments of courts of the United States predicated upon the civil liability provisions of the federal securities laws of the United States or any state; and (ii) in original actions brought in the Cayman Islands, to impose liabilities against us predicated upon the civil liability provisions of the federal securities laws of the United States or any state, so far as the liabilities imposed by those provisions are penal in nature. In those circumstances, although there is no statutory enforcement in the Cayman Islands of judgments obtained in the United States, the courts of the Cayman Islands will recognize and enforce a foreign money judgment of a foreign court of competent jurisdiction without retrial on the merits based on the principle that a judgment of a competent foreign court imposes upon the judgment debtor an obligation to pay the sum for which judgment has been given provided certain conditions are met. For a foreign judgment to be enforced in the Cayman Islands, such judgment must be final and conclusive and for a liquidated sum, and must not be in respect of taxes or a fine or penalty, inconsistent with a Cayman Islands judgment in respect of the same matter, impeachable on the grounds of fraud or obtained in a manner, and or be of a kind the enforcement of which is, contrary to natural justice or the public policy of the Cayman Islands (awards of punitive or multiple damages may well be held to be contrary to public policy). A Cayman Islands Court may stay enforcement proceedings if concurrent proceedings are being brought elsewhere.

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to the ordinary shares offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the ordinary shares offered hereby, we refer you to the registration statement and the exhibits and schedules filed thereto. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. Upon completion of this offering, we will be required to file periodic reports, proxy statements, and other information with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934. You may read and copy this information at the Public Reference Room of the Securities and Exchange Commission, 100 F Street, N.E., Room 1580, Washington, District of Columbia, 20549. You may obtain information on the operation of the public reference rooms by calling the Securities and Exchange Commission at 1-800-SEC-0330. The Securities and Exchange Commission also maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the Securities and Exchange Commission. The address of that site is [www.sec.gov](http://www.sec.gov).



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## Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of MeiraGTx Limited and Subsidiaries

### Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of MeiraGTx Limited and Subsidiaries (the Company) as of December 31, 2017 and 2016, the related consolidated statements of operations and comprehensive loss, convertible preferred C shares, shareholders' deficit and cash flows for each of the two years in the period ended December 31, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

### The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations, is subject to significant uncertainty with respect to its product development and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

### Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2016.

Stamford, Connecticut

March 29, 2018, except for Note 6, as to which the date is May 11, 2018

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**CONSOLIDATED BALANCE SHEETS**

	<u>December 31,</u> <u>2016</u>	<u>December 31,</u> <u>2017</u>	<u>March 31, 2018</u> <u>(unaudited)</u>
<b>ASSETS</b>			
<b>CURRENT ASSETS:</b>			
Cash and cash equivalents	\$ 17,476,641	\$ 8,548,638	\$ 32,356,851
Prepaid expenses	1,212,183	1,961,243	2,816,413
Other current assets	400,956	965,233	841,172
Total Current Assets	<u>19,089,780</u>	<u>11,475,114</u>	<u>36,014,436</u>
Property and equipment, net	3,016,525	14,255,729	14,643,091
Restricted cash	444,844	123,376	123,376
<b>TOTAL ASSETS</b>	<u><b>\$ 22,551,149</b></u>	<u><b>\$ 25,854,219</b></u>	<u><b>\$ 50,780,903</b></u>
<b>LIABILITIES, CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' DEFICIT</b>			
<b>CURRENT LIABILITIES:</b>			
Accounts payable	\$ 1,474,213	\$ 7,055,380	\$ 5,184,508
Accrued expenses	4,018,103	9,332,944	6,657,257
Note payable	—	1,442,009	—
Warrant liability	—	2,679,633	2,010,225
Capitalized lease obligation—current portion	6,015	30,850	28,715
Due to Kadmon	543,038	861,030	6,493
Total Current Liabilities	<u>6,041,369</u>	<u>21,401,846</u>	<u>13,887,198</u>
Capitalized lease obligation	5,458	34,298	28,655
Deferred rent	588,491	266,290	241,488
Other liabilities	221,254	178,419	187,848
<b>TOTAL LIABILITIES</b>	<u><b>6,856,572</b></u>	<u><b>21,880,853</b></u>	<u><b>14,345,189</b></u>
<b>COMMITMENTS</b>			
<b>CONVERTIBLE PREFERRED C SHARES</b>			
Convertible Preferred C Shares 6,111,526, 19,428,037 and 36,330,692 issued and outstanding at December 31, 2016 and 2017 and March 31, 2018 (unaudited), respectively (liquidation preference of \$33,002,240, \$52,455,700 and \$98,092,869 at December 31, 2016 and 2017 and March 31, 2018 (unaudited), respectively)	<u>32,833,660</u>	<u>51,338,631</u>	<u>97,351,080</u>
<b>SHAREHOLDERS' DEFICIT:</b>			
A Ordinary Shares, \$0.00001 nominal value	342	342	364
34,224,578 issued and 32,712,995 issued and outstanding at December 31, 2016			
34,254,578 issued and 33,821,221 issued and outstanding at December 31, 2017			
36,389,760 issued and 36,235,113 issued and outstanding at March 31, 2018 (unaudited)			
Capital in excess of nominal value	17,900,995	20,080,713	23,691,708
Accumulated other comprehensive loss	(661,112)	(2,022,477)	(2,780,242)
Accumulated deficit	<u>(34,379,308)</u>	<u>(65,423,843)</u>	<u>(81,827,196)</u>
Total Shareholders' Deficit	<u>(17,139,083)</u>	<u>(47,365,265)</u>	<u>(60,915,366)</u>
<b>TOTAL LIABILITIES, CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' DEFICIT</b>	<u><b>\$ 22,551,149</b></u>	<u><b>\$ 25,854,219</b></u>	<u><b>\$ 50,780,903</b></u>

See Notes to Consolidated Financial Statements

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**

	<u>For the Years Ended</u>		<u>For the Three-Month</u>	
	<u>2016</u>	<u>December 31,</u> <u>2017</u>	<u>Periods Ended</u> <u>March 31,</u> <u>2017</u>	<u>2018</u>
			(unaudited)	(unaudited)
Operating expenses:				
General and administrative	6,026,529	9,325,017	2,148,540	11,122,016
Research and development	14,037,918	22,359,712	4,823,357	6,927,322
Total operating expenses	<u>20,064,447</u>	<u>31,684,729</u>	<u>6,971,897</u>	<u>18,049,338</u>
Loss from operations	(20,064,447)	(31,684,729)	(6,971,897)	(18,049,338)
Other non-operating income (expense)				
Foreign currency gain	265,543	1,676,117	149,249	978,624
Convertible note inducement expense	—	(553,500)	—	—
Change in fair value of warrant liability	—	(465,633)	—	669,408
Interest income	32,068	26,073	10,389	25,308
Interest expense	(25,440)	(42,863)	(8,126)	(27,355)
Net loss	(19,792,276)	(31,044,535)	(6,820,385)	(16,403,353)
Net loss attributable to the non-controlling interest in subsidiary	305,883	—	—	—
Net loss attributable to MeiraGTx Limited shareholders	(19,486,393)	(31,044,535)	(6,820,385)	(16,403,353)
Other comprehensive loss	(671,391)	(1,361,365)	(130,895)	(757,765)
Comprehensive loss	(20,157,784)	(32,405,900)	(6,951,280)	(17,161,118)
Less: comprehensive loss attributable to noncontrolling interest	8,520	—	—	—
Comprehensive loss attributable to MeiraGTx Limited shareholders	<u>\$ (20,149,264)</u>	<u>\$ (32,405,900)</u>	<u>\$ (6,951,280)</u>	<u>\$ (17,161,118)</u>
Net loss attributable to MeiraGTx Limited shareholders	<u>\$ (19,486,393)</u>	<u>\$ (31,044,535)</u>	<u>\$ (6,820,385)</u>	<u>\$ (16,403,353)</u>
Accretion on convertible preferred C shares	(85,425)	(806,963)	(22,761)	(664,718)
Adjusted net loss attributable to MeiraGTx Limited ordinary shareholders	<u>\$ (19,571,818)</u>	<u>\$ (31,851,498)</u>	<u>\$ (6,843,146)</u>	<u>\$ (17,068,071)</u>
Basic and diluted net loss per ordinary share attributable to ordinary shareholders	<u>\$ (0.63)</u>	<u>\$ (0.96)</u>	<u>\$ (0.21)</u>	<u>\$ (0.49)</u>
Weighted-average number of ordinary shares outstanding	<u>31,098,591</u>	<u>33,269,157</u>	<u>32,851,408</u>	<u>34,647,368</u>

See Notes to Consolidated Financial Statements

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' DEFICIT**  
**AS OF MARCH 31, 2018**

	Convertible Preferred C Shares		Shareholders' Deficit							
	Convertible Preferred C Shares	Amount	A Ordinary Shares	B Ordinary Shares	Amount	Capital in Excess of Nominal Value	Accumulated Other Comprehensive Income (Loss)	Non-Controlling Interest in Subsidiary	Accumulated Deficit	Shareholders' Deficit
Balance at December 31, 2015	1,944,440	\$ 10,416,205	29,851,230	10,000	\$ 299	\$ 15,594,166	\$ 1,759	\$ (789,698)	\$(14,892,915)	\$ (86,389)
Issuance of A ordinary shares in connection with the Acquisition of BRI-Alzan, Inc.	—	—	300,000	—	3	597,297	—	—	—	597,300
Issuance of A ordinary shares in connection with acquisition of non-controlling interest of MeiraGTX UK II Limited	—	—	4,017,048	—	40	(1,104,141)	—	1,104,101	—	—
Issuance of convertible preferred C shares in connection with a payable	230,000	1,242,000	—	—	—	—	—	—	—	—
Issuance of A ordinary shares in connection with a consulting agreement	—	—	46,300	—	—	92,137	—	—	—	92,137
Conversion of B ordinary shares into A ordinary shares	—	—	10,000	(10,000)	—	—	—	—	—	—
Issuance of convertible preferred C shares in connection with a research agreement	59,259	319,999	—	—	—	—	—	—	—	—
Issuance of convertible preferred C shares, net of issuance costs	3,877,827	20,770,031	—	—	—	—	—	—	—	—
Accretion of issuance costs on convertible preferred C shares	—	85,425	—	—	—	(85,425)	—	—	—	(85,425)
Share-based compensation	—	—	—	—	—	2,806,961	—	—	—	2,806,961
Foreign currency translation	—	—	—	—	—	—	(662,871)	(8,520)	—	(671,391)
Net loss for the year ended December 31, 2016	—	—	—	—	—	—	—	(305,883)	(19,486,393)	(19,792,276)
Balance at December 31, 2016	6,111,526	\$ 32,833,660	34,224,578	—	\$ 342	\$ 17,900,995	\$ (661,112)	\$ —	\$(34,379,308)	\$(17,139,083)
Exercised stock options	—	—	5,000	—	—	9,950	—	—	—	9,950
Issuance of A ordinary shares in connection with a license agreement	—	—	25,000	—	—	17,000	—	—	—	17,000
Extinguishment of convertible preferred C shares, net of unaccreted issuance costs	(6,149,326)	(33,115,157)	—	—	—	33,115,157	—	—	—	33,115,157
Issuance of convertible preferred C shares in connection with extinguishment	12,298,652	33,206,360	—	—	—	(33,206,360)	—	—	—	(33,206,360)
Conversion of note payable into convertible preferred C shares	925,926	2,500,000	—	—	—	—	—	—	—	—
Issuance of convertible preferred C shares, net of warrants and issuance costs	6,241,259	15,198,008	—	—	—	—	—	—	—	—
Accretion of issuance costs on convertible preferred C shares	—	100,760	—	—	—	(100,760)	—	—	—	(100,760)
Accretion of warrants issued in connection with convertible preferred C shares	—	615,000	—	—	—	(615,000)	—	—	—	(615,000)
Share-based compensation	—	—	—	—	—	2,959,731	—	—	—	2,959,731
Foreign currency translation	—	—	—	—	—	—	(1,361,365)	—	—	(1,361,365)
Net loss for the year ended December 31, 2017	—	—	—	—	—	—	—	—	(31,044,535)	(31,044,535)
Balance at December 31, 2017	19,428,037	51,338,631	34,254,578	—	\$ 342	\$ 20,080,713	\$ (2,022,477)	\$ —	\$(65,423,843)	\$(47,365,265)
Issuance of convertible preferred C shares in connection with payables	502,270	1,356,129	—	—	—	—	—	—	—	—
Issuance of preferred C shares in connection with a license agreement	51,852	140,000	—	—	—	—	—	—	—	—
Issuance of convertible preferred C shares, net of issuance costs	16,348,533	43,851,602	—	—	—	—	—	—	—	—
Accretion of issuance costs on convertible preferred C shares	—	94,445	—	—	—	(94,445)	—	—	—	(94,445)
Accretion of warrants issued in connection with convertible preferred C shares	—	570,273	—	—	—	(570,273)	—	—	—	(570,273)
Share-based compensation	—	—	2,135,182	—	22	4,275,713	—	—	—	4,275,735
Foreign currency translation	—	—	—	—	—	—	(757,765)	—	—	(757,765)
Net loss for the three-month period ended March 31, 2018	—	—	—	—	—	—	—	—	(16,403,353)	(16,403,353)
Balance at March 31, 2018 (unaudited)	36,330,692	\$ 97,351,080	36,389,760	—	\$ 364	\$ 23,691,708	\$ (2,780,242)	\$ —	\$(81,827,196)	\$(60,915,366)

See Notes to Consolidated Financial Statements

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**

	<b>For the Year Ended</b>		<b>For the Three-Month</b>	
	<b>December 31,</b>		<b>Period Ended March 31,</b>	
	<b>2016</b>	<b>2017</b>	<b>2017</b>	<b>2018</b>
			<b>(unaudited)</b>	<b>(unaudited)</b>
<b>Cash flows from operating activities:</b>				
Net loss	\$ (19,792,276)	\$ (31,044,535)	\$ (6,820,385)	\$ (16,403,353)
<b>Adjustments to reconcile net loss to net cash used in operating activities:</b>				
Issuance of shares for services	443,136	17,000	—	—
Share-based compensation expense	2,806,961	2,959,731	844,237	4,275,735
Foreign currency loss (gain)	(261,817)	(1,676,117)	(149,249)	(978,624)
Depreciation	243,081	679,177	179,878	458,836
Amortization of interest on asset retirement obligation	17,248	19,313	4,507	3,678
Change in fair value of warrant liability	—	465,633	—	(669,408)
Convertible note inducement expense	—	553,500	—	—
Acquired research and development expense	597,300	—	—	—
Issuance of note payable in connection with lease termination	—	1,442,009	—	—
Preferred C shares issued in connection with a license agreement	—	—	—	140,000
(Increase) decrease in operating assets:				
Prepaid expenses and other current assets	(960,993)	(669,756)	(122,914)	(821,062)
Other current assets	(302,901)	(493,424)	(338,126)	153,773
Increase (decrease) in operating liabilities:				
Accounts payable	453,130	4,728,491	842,876	171,045
Accrued expenses	1,333,796	4,969,619	(1,147,336)	(2,846,292)
Due to Kadmon	800,223	317,992	(128,974)	(854,537)
Deferred rent	255,160	(324,019)	389,928	(25,760)
Other liabilities	—	—	50,220	—
<b>Net cash used in operating activities</b>	<b>(14,367,952)</b>	<b>(18,055,386)</b>	<b>(6,395,338)</b>	<b>(17,395,969)</b>
<b>Cash flows from investing activities:</b>				
Purchase of property and equipment	(2,593,584)	(10,535,717)	(1,737,520)	(1,210,452)
<b>Net cash used in investing activities</b>	<b>(2,593,584)</b>	<b>(10,535,717)</b>	<b>(1,737,520)</b>	<b>(1,210,452)</b>
<b>Cash flows from financing activities:</b>				
Payments on capitalized lease obligation	(5,480)	(24,388)	(1,452)	(7,779)
Proceeds from the issuance of note payable	—	2,500,000	—	—
Proceeds from the issuance of convertible preferred C shares, net of issuance costs	20,762,682	16,854,653	197,995	43,851,602
Proceeds from exercised stock options	—	9,950	—	—
Payment of note payable	—	—	—	(1,442,009)
<b>Net cash provided by financing activities</b>	<b>20,757,202</b>	<b>19,340,215</b>	<b>196,543</b>	<b>42,401,814</b>
Net increase (decrease) in cash, cash equivalents and restricted cash	3,795,666	(9,250,888)	(7,936,315)	23,795,393
Effect of exchange rate changes on cash	(421,240)	1,417	(11,109)	12,820
Cash, cash equivalents and restricted cash at beginning of period	14,547,059	17,921,485	17,921,485	8,672,014
Cash, cash equivalents and restricted cash at end of period	<u>\$ 17,921,485</u>	<u>\$ 8,672,014</u>	<u>\$ 9,974,061</u>	<u>\$ 32,480,227</u>
<b>Supplemental disclosure of non-cash transactions:</b>				
Fixed asset acquisition included in accounts payable and accrued expenses	\$ 301,655	\$ 415,650	\$ 766,107	\$ (811,095)
Conversion of note payable into convertible preferred C shares	\$ —	\$ 2,500,000	\$ —	\$ —
Issuance of convertible preferred C shares in connection with payables	\$ —	\$ —	\$ —	\$ 1,356,129
Capitalized lease obligation for equipment purchase	\$ 17,817	\$ 78,063	\$ —	\$ —
Issuance of convertible preferred C shares in settlement of due to Kadmon	\$ 1,242,000	\$ —	\$ —	\$ —
Issuance of A ordinary shares for acquisition of BRI-Alzan	\$ 597,300	\$ —	\$ —	\$ —
Issuance of convertible preferred C shares in connection with a research agreement	\$ 320,000	\$ —	\$ —	\$ —
Asset retirement obligation in connection with a lease	\$ 205,659	\$ (75,011)	\$ —	\$ —
<b>Supplemental disclosure of cash flow information:</b>				
Cash paid for interest	\$ —	\$ 20,894	\$ 257	\$ 31,531

See Notes to Consolidated Financial Statements

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**1. Principal Business Activity:**

***The Company***

MeiraGTx Limited (the “Company” or “Meira Limited”), a limited company under the laws of England and Wales formed on March 20, 2015, is a clinical-stage biotech company developing novel gene therapy treatments for a wide range of inherited and acquired disorders for which there are no effective treatments available. The Company is focused on developing therapies for ocular diseases, including rare inherited blindness as well as Xerostomia following radiation treatment for head and neck cancers and neurodegenerative diseases such as amyotrophic lateral sclerosis (“ALS”).

On April 24, 2015, the Company acquired certain assets held by Kadmon Corporation, LLC (“Kadmon”) and began operations. In connection with the transfer of these assets, the Company entered into a transition services agreement with Kadmon whereby Kadmon would provide office and laboratory facilities as well as certain other personnel support activities (see Note 14).

On April 27, 2015, the Company entered into a worldwide collaborative development and license agreement (“CDLA”) with Athena Vision Limited (“Athena”) to develop and commercialize pre-clinical gene therapies for certain ocular indications. Concurrent with the execution of the CDLA, the Company and Athena entered into a shareholders’ agreement in which the Company issued 2,760,000 A ordinary shares (“Ordinary Shares”) and 250 B ordinary shares, which were converted into Ordinary Shares, to the shareholders of Athena in exchange for a 60% equity interest in Athena.

On April 8, 2016, the Company issued 4,017,048 Ordinary Shares to the shareholders of Athena in exchange for the remaining 40% equity interest in Athena and changed the name of Athena to MeiraGTx UK II Limited (“MeiraGTx UK II”).

***Basis of Presentation***

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (“GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Update (“ASU”) of the Financial Accounting Standards Board (“FASB”).

On April 27, 2015, the Company acquired as 60% interest in MeiraGTx UK II. As such, a non-controlling interest was recorded on the date of acquisition through April 8, 2016, when the Company acquired the remaining 40% interest in MeiraGTx UK II.

***Liquidity***

The consolidated financial statements of the Company have been prepared on a going-concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. Accordingly, the financial statements do not include any adjustments that might be necessary should the Company be unable to continue in existence. The Company has not generated any revenues and has not yet achieved profitable operations. There is no assurance that profitable operations, if ever achieved, could be sustained on a continuing basis. In addition, development activities, clinical and preclinical testing, and commercialization of the Company’s product candidates will require significant additional financing. The Company’s accumulated deficit at December 31, 2017 and March 31, 2018 totaled \$65,423,843 and \$81,827,196,

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

respectively, and management expects to incur substantial and increasing losses in future periods. The success of the Company is subject to certain risks and uncertainties, including among others, uncertainty of product development; competition in the Company's field of use; uncertainty of capital availability; uncertainty in the Company's ability to enter into agreements with collaborative partners; dependence on third parties; and dependence on key personnel. The Company has not generated positive cash flows from operations, and there are no assurances that the Company will be successful in obtaining an adequate level of financing for the development and commercialization of its product candidates. These factors raise substantial doubt about the Company's ability to continue as a going concern. The Company does not have adequate cash on hand to cover its anticipated expenses past the next 12 months. If the Company fails to raise a significant amount of capital or enter into a strategic transaction, it may need to significantly curtail operations, cease operations or seek federal bankruptcy protection in the near future. These conditions raise substantial doubt about its ability to continue as a going concern.

As of December 31, 2017, the Company had cash and cash equivalents in the amount of \$8,548,638, which consisted of depository accounts. From January 1, 2018 through March 29, 2018, the Company issued 16,943,396 convertible preferred C shares ("Preferred Shares") for gross proceeds of \$45,747,173. The Company estimates that its cash and cash equivalents on hand at December 31, 2017 and the proceeds from the issuance of Preferred Shares from January 1, 2018 through March 29, 2018 will cover its expenses into the fourth quarter of 2018.

As of March 31, 2018, the Company had cash and cash equivalents in the amount of \$32,356,851, which consisted of depository accounts. From April 1, 2018 through April 30, 2018, the company issued 4,597,637 Preferred Shares for gross proceeds of \$12,413,619. The Company estimates that its cash and cash equivalents on hand at March 31, 2018 and the proceeds from the issuance of Preferred Shares from April 1, 2018 through April 30, 2018 will cover its expenses into the first quarter of 2019.

In order to provide the Company with the cash resources necessary to fund operations, the Company will continue its efforts to raise additional capital through either a private or public equity placement or strategic transaction in the near future.

If the Company is unable to raise additional funds, it will need to do one or more of the following:

- license third parties to develop and commercialize products or technologies that it would otherwise seek to develop and commercialize itself;
- seek strategic alliances or business combinations;
- attempt to sell the Company;
- cease operations; or
- declare bankruptcy.

***Risks and Uncertainties***

The Company operates in an industry that is subject to intense competition, government regulation and rapid technological change. The Company's operations are subject to significant risk and uncertainties including financial, operational, technological, regulatory and other risks, including the potential risk of business failure.



**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

The Company's limited capital resources and operations to date have been funded primarily with the proceeds from private equity.

***Reverse Stock Split***

The Company's shareholders approved a 10:1 stock split, effective February 2, 2016. All share information presented in these financial statements and accompanying footnotes have been retroactively adjusted to reflect the increased number of shares resulting from this action.

**2. Summary of Significant Accounting Policies:**

***Consolidation***

The accompanying condensed consolidated financial statements include the accounts of Meira Limited and its wholly owned subsidiaries:

MeiraGTX, LLC, a Delaware corporation, ("Meira LLC");

BRI-Alzan, Inc., a Delaware corporation ("BRI-Alzan");

MeiraGTX B.V., a Netherlands corporation ("Meira BV");

MeiraGTX UK II Limited, ("Meira UK II"), a limited company under the laws of England and Wales;

MeiraGTX UK Limited ("Meira UK"), a limited company under the laws of England and Wales.

All intercompany balances and transactions between the consolidated companies have been eliminated in consolidation.

***Unaudited Interim Financial Statements***

The accompanying interim consolidated balance sheet as of March 31, 2018, the consolidated statements of operations and comprehensive loss and consolidated statements of cash flows for the three months ended March 31, 2017 and 2018, the statement of convertible preferred C shares and stockholders' deficit for the three months ended March 31, 2018, and the financial data and other information disclosed in these notes related to the three months ended March 31, 2017 and 2018 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the audited annual financial statements, and, in the opinion of management, reflect all adjustments, consisting of normal recurring adjustments, necessary for the fair presentation of the Company's financial position as of March 31, 2018, and the results of its operations and its cash flows for the three month ended March 31, 2017 and 2018. The results as of and for the three months ended March 31, 2018 are not necessarily indicative of the results to be expected for the year ending December 31, 2018, any other interim periods, or any future year or period.

***Use of Estimates***

Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these consolidated financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. In preparing these consolidated financial statements, management used significant estimates in the following areas, among others: valuation of Ordinary Shares issued for the acquisition of assets, the accounting for research and development costs, warrants, share based compensation and accrued expenses.

***Subsequent Events***

The Company considers events or transactions that occur after the balance sheet date but before the financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. Subsequent events were reviewed through the date of this filing for the years ended December 31, 2016 and 2017 and for the interim financial statements and disclosures for the three months ended March 31, 2017 and 2018. See Note 17 for additional information.

***Cash and Cash Equivalents***

The Company considers all highly liquid instruments with an original maturity of 90 days or less at the time of purchase to be cash equivalents. Cash and cash equivalents consist of deposits that are readily convertible into cash.

***Warrant Liability***

During 2017, the Company issued warrants to purchase Preferred Shares to certain investors. Due to the potential redemption feature of the underlying Preferred Shares, the warrants have been classified as a liability. Liability accounting requires that the fair value of warrants be remeasured each reporting period with changes recorded in the statements of operations and comprehensive loss. These Preferred Shares warrants will remain outstanding until the exercise or expiration of the warrants or the completion of a qualified IPO, at which time the warrant liability will be remeasured to fair value and reclassified to additional paid-in capital.

***Financial Instruments***

The carrying value of prepaid expenses, other current assets, accounts payable, accrued expenses, notes payable and amounts due to an affiliate reported in the consolidated balance sheets equal or approximate fair value due to their short maturities.

***Fair Value Measurements***

Fair value is defined as the price that would be received upon sale of an asset or paid upon transfer of a liability in an orderly transaction between market participants at the measurement date and in the principal or most advantageous market for that asset or liability. The fair value should be calculated based on assumptions that market participants would use in pricing the asset or liability, not on assumptions specific to the entity. In addition, the fair value of liabilities should include consideration of non-performance risk including our own credit risk.

The Company follows ASC Topic 820, *Fair Value Measurements and Disclosures*, or ASC 820, for application to financial assets. In addition to defining fair value, the standard expands the disclosure requirements

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

around fair value and establishes a fair value hierarchy for valuation inputs. The hierarchy prioritizes the inputs into three levels based on the extent to which inputs used in measuring fair value are observable in the market. Each fair value measurement is reported in one of the three levels which are determined by the lowest level input that is significant to the fair value measurement in its entirety. These levels are:

- Level 1: Observable inputs such as quoted prices in active markets for identical assets the reporting entity has the ability to access as of the measurement date;
- Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly; and
- Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The table below represents the values of the Company's financial assets and liabilities that are required to be measured at fair value on a recurring basis:

<u>Description</u>	December 31, 2016	Fair Value Measurement Using:		Significant Unobservable (Level 3)
		Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	
Restricted cash	\$ 444,844	\$ 444,844	\$ —	\$ —
Total	\$ 444,844	\$ 444,844	\$ —	\$ —

<u>Description</u>	December 31, 2017	Fair Value Measurement Using:		Significant Unobservable (Level 3)
		Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	
Restricted cash	\$ 123,376	\$ 123,376	\$ —	\$ —
Warrants	2,679,633	—	—	2,679,633
Total	\$ 2,803,009	\$ 123,376	\$ —	\$ 2,679,633

<u>Description</u>	March 31, 2018	Fair Value Measurement Using:		Significant Unobservable (Level 3)
		Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	
Restricted cash	\$ 123,376	\$ 123,376	\$ —	\$ —
Warrants	2,010,225	—	—	2,010,225
Total	\$ 2,133,601	\$ 123,376	\$ —	\$ 2,010,225

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

The table below represents a rollforward of the assets and liabilities that are required to be measured at fair value on a recurring basis from December 31, 2015 to March 31, 2018:

	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Balance as of December 31, 2015	\$ —	\$ —	\$ —
Restriction of cash	444,844	—	—
Balance as of December 31, 2016	444,844	—	—
Cash released from restriction	(321,468)	—	—
Fair value of warrants issued	—	—	2,214,000
Change in fair value of warrants	—	—	465,633
Balance as of December 31, 2017	123,376	—	2,679,633
Change in fair value of warrants	—	—	(669,408)
Balance as of March 31, 2018	<u>\$ 123,376</u>	<u>\$ —</u>	<u>\$ 2,010,225</u>

The warrants are classified as liabilities because the underlying Preferred Shares have a redemption feature in the event of a change of control of the Company.

The fair values of the warrants were estimated using the Black-Scholes valuation model with the following assumptions:

	<u>September 21, 2017</u>	<u>November 2, 2017</u>	<u>December 31, 2017</u>	<u>March 31, 2018</u>
Risk-free interest rate	1.38%	1.53%	1.72%	1.86%
Expected volatility	80%	80%	80%	80%
Expected dividend yield	0	0	0	0
Expected life	18 months	18 months	9 months	5.5 months

For the unobservable inputs for the warrants, the expected volatility was determined at each measurement date by taking an average of the volatility of other publicly-traded peer biotechnology companies. The expected life was determined at each measurement date based upon the Company's estimate of the time until the Company has a conversion event, as described in Note 11.

The fair value of the Preferred Shares was based upon recent issuances of the Company's Preferred Shares on or about these dates.

The estimated fair values of the Company's warrants are not necessarily indicative of the amounts that would be realized in a current market exchange. The determination of the fair value of the warrants are sensitive to changes in the assumptions used and a change in those inputs could result in a significantly higher or lower fair value measurement. If the volatility were to increase or the expected life were to increase, the fair value of the warrant would increase. Conversely, if the volatility were to decrease or the expected life were to decrease, the fair value of the warrant would decrease.

***Convertible Preferred C Shares***

The Preferred Shares are not redeemable. However, in the event of a Sale (as defined in the Company's Articles of Association), which would include a change of control that is outside of the Company's control, the Preferred Shares are entitled to receive a payment which is equal to their liquidation value. The feature is being accounted for as a redemption under ASC 480.

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The Company is accounting for its Preferred Shares under the requirements of ASC 480 which establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. The carrying value of the Preferred Shares is presented in as temporary equity and is increased by periodic accretions so that the carrying amount will equal the redemption amount at the estimated date that the Preferred Shares will be converted into Ordinary Shares. These increases are affected through charges against additional paid-in capital, to the extent it is available, or accumulated deficit. For all Preferred Shares issuance, the difference between the amount invested by the holders of the Preferred Shares, net of issuance costs and the initial fair value of warrants issued in connection with the Preferred Shares (if applicable) and the liquidation value of the Preferred Shares is recorded as accretion over the estimated life of the Preferred Shares. The accretion is added to net loss to arrive at the net loss available to Ordinary Shareholders in the calculation of loss per Ordinary Share.

***Concentrations of Credit Risk***

The Company maintains its cash and cash equivalents primarily in depository and money market accounts within two large financial institutions in the United States and one large financial institution in the United Kingdom. Cash balances deposited at these major financial banking institutions exceed the insured limit. The Company has not experienced any losses on its bank deposits and believes these deposits do not expose the Company to any significant credit risk.

***Property and Equipment, Net***

Property and equipment (consisting of computer, office, laboratory and manufacturing equipment, furniture and fixtures and leasehold improvements) are stated at cost, net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the respective assets. Leasehold improvements are depreciated over the lesser of their useful lives or the life of the lease (see Note 5).

The estimated useful lives of the asset categories are set forth in the table below:

<u>Asset Category</u>	<u>Useful Lives</u>
Computer and office equipment	3 years
Laboratory equipment	5 years
Manufacturing equipment	7 years
Furniture and fixtures	5 years
Leasehold improvements	lesser of useful life or remaining term of lease

Expenditures for leasehold improvements are capitalized, and expenditures for maintenance and repairs are expensed to operations as incurred.

ASC Topic 360, *Property, Plant and Equipment*, addresses the financial accounting and reporting for impairment or disposal of long-lived assets. The Company reviews the recorded values of long-lived assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of an asset or group of assets may not be fully recoverable. The Company recorded no impairment charges in any of the periods presented.

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***Net Loss per Ordinary Share***

Basic net loss per Ordinary Share is computed by dividing net loss attributable to the Company's shareholders by the weighted average number of shares of the Company's Ordinary Shares assumed to be outstanding during the period of computation. Diluted net loss per ordinary share is computed similar to basic net loss per share except that the denominator is increased to include the number of additional Ordinary Shares that would have been outstanding if the potential ordinary shares had been issued at the beginning of the year and if the additional ordinary shares were dilutive (treasury stock method) or the two-class method, whichever is more dilutive. For all period presented, basic and diluted net loss per Ordinary Share are the same, as any additional Ordinary Share equivalents would be anti-dilutive (see Note 12).

***Income Taxes***

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes*, or ASC 740, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Realization of net deferred tax assets is dependent on future taxable income. Valuation allowances are provided, if based upon the weight of available evidence, it is more likely than not that some, or all, of the deferred tax assets will not be realized. Realization of net deferred tax assets is dependent on future taxable income (see Note 13).

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2016 and 2017, the Company does not have any significant uncertain tax positions.

The Company is required to estimate income taxes in each of the jurisdictions in which it operates.

The Company's reserves related to taxes are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized. As of December 31, 2017, the Company had no unrecognized tax benefits or related interest and penalties accrued.

In the United States, on December 22, 2017, the "Tax Cuts and Jobs Act" (the "Act") was signed into law. Substantially all of the provisions of the Act are effective for taxable years beginning after December 31, 2017. The Act includes significant changes to the Internal Revenue Code of 1986 (as amended, the "Code"), including amendments which significantly change the taxation of individuals, and business entities. The Act contains numerous provisions impacting the Company, the most significant of which reduces the Federal corporate statutory tax rate from 34% to 21%.

The staff of the U.S. Securities and Exchange Commission ("SEC") has recognized the complexity of reflecting the impacts of the Act, and on December 22, 2017 issued guidance in Staff Accounting Bulletin 118 ("SAB 118"), which clarifies accounting for income taxes under ASC 740 if information is not yet available or complete and provides for up to a one year period in which to complete the required analyses and accounting (the measurement period). SAB 118 describes three scenarios (or "buckets") associated with a company's status of accounting for income tax reform: (1) a company is complete with its accounting for certain effects of tax

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reform, (2) a company is able to determine a reasonable estimate for certain effects of tax reform and records that estimate as a provisional amount, or (3) a company is not able to determine a reasonable estimate and therefore continues to apply ASC 740, based on the provisions of the tax laws that were in effect immediately prior to the Act being enacted.

The various provisions under the Act deemed most relevant to the Company have been considered in preparation of its financial statements as of December 31, 2017. The Company has made a reasonable estimate for certain effects of tax reform and has recorded provisional amounts as part of its income tax provision. To the extent that clarifications or interpretations materialize in the future that would impact upon the effects of the Act incorporated into the December 31, 2017 financial statements, those effects will be reflected in the future as or if they materialize.

Through March 31, 2018, the Company did not have any significant adjustments to the provisional amounts. The Company will continue to analyze the provisional amounts, which are still subject to change during the measurement period, and the Company anticipates further guidance on accounting interpretations from the FASB and application of the law from the Department of the Treasury.

***Research and Development***

Research and development costs are charged to expense as incurred. These costs include, but are not limited to, employee-related expenses, including salaries, benefits and travel of the Company's research and development personnel; expenses incurred under agreements with contract research organizations and investigative sites that conduct clinical and preclinical studies and manufacture the drug product for the clinical studies and preclinical activities; acquisition of in-process research and development; facilities; supplies; rent, insurance, certain legal fees, stock-based compensation, depreciation and other costs associated with clinical and preclinical activities and regulatory operations. Refundable research and development tax credits received are recorded as an offset to these costs.

Costs for certain development activities, such as outside research programs funded by the Company, are recognized based on an evaluation of the progress to completion of specific tasks with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.

***Share Based Compensation Expense***

*Options*

The Company grants share options to employees, non-employee members of the Company's board of directors and non-employee consultants as compensation for services performed. Employee and non-employee members of the board of directors' awards of share-based compensation are accounted for in accordance with ASC 718, *Compensation - Stock Compensation* or ASC 718. ASC 718 requires all share-based payments to employees and non-employee directors, including grants of share options, to be recognized in the Statement of Operations and Comprehensive Loss based on their grant date fair values. The grant date fair value of share options is estimated using the Black-Scholes option valuation model.

Using this model, fair value is calculated based on assumptions with respect to (i) the fair value of the Company's Ordinary Shares on the grant date; (ii) expected volatility of the Company's Ordinary Share price,

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(iii) the periods of time over which employees and members of the Company's board of directors are expected to hold their options prior to exercise (expected term), (iv) expected dividend yield on the Company's Ordinary Shares, and (v) risk-free interest rates.

As there has been no public market for the Company's Ordinary Shares to date, the estimated fair value of the Ordinary Shares has been determined by the Company's board of directors as of the date of each option grant, with input from management, considering the most recently available third-party valuations of Ordinary Shares and the board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant.

The third party estimated the fair value of the equity using a special case of the market approach known as the backsolve method. The backsolve method was used to solve for the implied total equity value based on the Company's recent Series C financing round. Consideration was given to the rights and preferences of each of Company's classes of equity and the expected time to a liquidity event. An option pricing allocation method, or OPM, was selected to allocate the total equity value. The OPM treats ordinary shares and preferred shares as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the Ordinary Shares have value only if the funds available for distribution to stockholders exceeded the value of the Preferred Share liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. These third-party valuations resulted in a valuation of the Company's Ordinary Shares of \$1.95, \$0.68, \$1.45 and \$1.55 per share as of December 31, 2016, September 15, 2017, December 31, 2017 and March 31, 2018, respectively.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if the Company had used different assumptions or estimates, the fair value of its Ordinary Shares and its share-based compensation expense could have been materially different.

Since Company's Ordinary Shares have not been traded on a public exchange, the Company believes that it does not have sufficient company-specific information available to determine the expected term based on its historical data. As a result, the expected term of share options granted to employees and members of the Company's board of directors is determined using the average of the vesting period and contractual life of the option, an accepted method for the Company's option grants under the SEC's Staff Accounting Bulletin No. 107 and No. 110, *Share-Based Payment*.

Similarly, the Company believes that its future volatility will differ materially during the expected term from the volatility that would be calculated from its historical share prices to date. Consequently, expected volatility is based on an analysis of guideline companies in accordance with ASC 718. The expected dividend yield is zero as the Company has never paid dividends and does not currently anticipate paying any in the foreseeable future. Risk-free interest rates are based on quoted U.S. Treasury rates for securities with maturities approximating the option's expected term.

As of January 1, 2016, the Company early adopted ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting*, and accounts for forfeitures as they occur from that date. Additionally, excess tax benefits and deficiencies will be recognized as income tax expense or benefit in the income statement. There was no cumulative effect adjustment as the Company did not issue any options prior to January 1, 2016 (see *Accounting Pronouncements Recently Adopted*, below).

The Company accounts for options granted to non-employee consultants under ASC 505-50, *Equity-Based Payments to Non-Employees*. As such, the Company estimates the fair value of each such option using the



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Black-Scholes model, with the expected term of share options granted to non-employees initially equal to the options' maximum contractual life of ten years, at issuance. On each subsequent reporting date until performance is complete, the Company revalues all outstanding options granted to non-employee consultants during the vesting period of each tranche. Under ASC 505-50, upon re-measurement of each award, income or expense is recognized during its vesting term. Compensation cost relating to awards with service-based graded vesting schedules is recognized as general and administrative and research and development expenses in the consolidated statements of operations and comprehensive loss using the straight-line method.

*Restricted Shares*

In connection with certain service agreements and research agreements, the Company has granted restricted ordinary shares as compensation. The shares are recognized in the statements of operations and comprehensive loss based on their grant date fair values. Compensation cost relating to share grants with service-based graded vesting schedules is recognized based on the vesting schedule.

*Leases*

The Company recognizes rent expense for operating leases on a straight-line basis over the term of the lease, beginning on the date the Company takes possession of the property. Rent expense includes the base amounts stated in the lease agreement as well as the effect of reduced or free rent and rent escalations. At lease inception, the Company determines the lease term by assuming the exercise of those renewal options that are reasonably assured because of the significant economic penalty that exists for not exercising those options. The exercise of renewal options is at the Company's sole discretion. The expected lease term is one of the factors used to determine whether a lease is classified as operating or capital and is used to calculate the straight-line rent expense. The difference between the cash paid to the landlord and the amount recognized as rent expense on a straight-line basis is included in deferred rent and classified within long-term liabilities. Lease incentives made by landlords to or on behalf of the Company for leasehold improvements are recorded as deferred rent and classified as long-term liabilities.

The Company uses estimates to determine the amount of asset retirement obligation at the end of the lease terms and discounts such asset retirement obligations using an estimated discount rate. Interest on the discounted asset retirement obligation is amortized over the term of the lease using the effective interest method and is recorded as interest expense in the consolidated statements of operations and comprehensive loss.

*Asset Retirement Obligation*

Accounting for Asset Retirement Obligations requires legal obligations associated with the retirement of long-lived assets to be recognized at fair value when incurred and capitalized as part of the related long-lived asset. In the absence of quoted market prices, we estimate the fair value of our asset retirement obligations using Level 3 present value techniques, in which estimates of future cash flows associated with retirement activities are discounted using a credit-adjusted risk-free rate. Asset retirement obligations currently reported as other liabilities on our Consolidated Balance Sheet were measured during a period of historically low interest rates. The impact on measurements of new asset retirement obligations using different rates in the future may be significant.

The Company uses estimates to determine the amount of the asset retirement obligations at the end of the lease term and discounts such asset retirement obligations using an estimated discount rate. Interest on the discounted asset retirement obligation is amortized over the term of the lease using the effective interest method and is recorded as interest expense in the consolidated statements of operations and comprehensive loss.

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The change in asset retirement obligations is as follows:

	<u>For the year ended December 31,</u>		<u>For the three months ended</u>
	<u>2016</u>	<u>2017</u>	<u>March 31,</u>
			<u>2018</u>
Balance at beginning of year	\$ —	\$ 221,254	\$ 178,419
Inception of asset retirement obligation	205,659	—	—
Amortization of interest	17,248	19,313	3,678
Change in estimate	—	(75,011)	—
Effects of exchange rate	(1,653)	12,863	5,751
Balance at end of year	<u>\$ 221,254</u>	<u>\$ 178,419</u>	<u>\$ 187,848</u>

**Other Comprehensive Loss**

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources.

**Foreign Currencies**

The Company's consolidated financial statements are presented in U.S. dollars, the reporting currency of the Company. The financial position and results of operations of MeiraGTx UK II and MeiraGTx B.V. are measured using the foreign subsidiaries' local currency as the functional currency. MeiraGTx UK II cash accounts holding U.S. dollars are remeasured based upon the exchange rate at the date of remeasurement with the resulting gain or loss included in the consolidated statements of operations and comprehensive loss. Expenses of such subsidiaries have been translated into U.S. dollars at average exchange rates prevailing during the period. Assets and liabilities have been translated at the rates of exchange on the consolidated balance sheet dates. The resulting translation gain and loss adjustments are recorded directly as a separate component of Shareholders' equity and as Other comprehensive loss on the consolidated statements of operations and comprehensive loss.

**Segment Information**

Management has concluded it has a single reporting segment for purposes of reporting financial condition and results of operations.

The following table summarizes non-current assets by geographical area:

	<u>December 31, 2016</u>	<u>December 31, 2017</u>	<u>March 31, 2018</u>
United States	\$ 1,081,522	\$ 436,463	\$ 411,254
United Kingdom	2,379,847	13,942,642	14,355,213
	<u>\$ 3,461,369</u>	<u>\$ 14,379,105</u>	<u>\$ 14,766,467</u>

**Accounting Pronouncements Recently Adopted**

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718), Scope of Modification Accounting*. ASU 2017-09 provides guidance on the types of changes to the terms or conditions of share-based payment awards to which an entity would be required to apply modification

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accounting. ASU 2017-09 is applied prospectively to awards modified on or after the effective date. The Company adopted ASU 2017-09 on January 1, 2018. There were no modifications that had an impact on the Company's consolidated financial statements.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations (Topic 805), Clarifying the Definition of a Business*, or ASU 2017-01, that clarifies the definition of a business to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. ASU 2017-01 requires an entity to evaluate if substantially all of the fair value of the gross assets acquired or disposed of is concentrated in a single identifiable asset or a group of similar identifiable assets; if so, the set of transferred assets and activities is not a business. ASU 2017-01 also requires a business to include at least an input and one substantive process that together significantly contribute to the ability to create output and removes the evaluation of whether a market participant could replace missing elements. ASU 2017-01 should be applied prospectively and is effective for annual periods beginning after December 15, 2017 and interim periods within those annual periods. The adoption of ASU 2017-01 on January 1, 2018 did not have a material effect on its financial position, results of operations or cash flows.

In May 2016, the FASB issued ASU No. 2016-12, *Revenue from Contracts with Customers (Topic 606), Narrow-Scope Improvements and Practical Expedients*, or ASU 2016-12, which amends guidance in the new revenue standard, ASU No. 2014-09 *Revenue from Contracts with Customers (Topic 606)*, or ASU 2014-09, on collectability, noncash consideration, presentation of sales tax and transition. The amendments in ASU 2016-12 are effective for annual reporting periods beginning after December 15, 2017 (i.e., January 1, 2018), including interim periods within those reporting periods, which is the same as for ASU 2014-09, as amended by ASU No. 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, or ASU 2015-14. In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with Customers (Topic 606), Identifying Performance Obligations and Licensing*, or ASU 2016-10, which clarifies the principle for determining whether a good or service is "separately identifiable" from other promises in the contract and, therefore, should be accounted for as a separate performance obligation. In that regard, ASU 2016-10 requires that an entity determine whether its promise is to transfer individual goods or services to the customer, or a combined item (or items) to which the individual goods and services are inputs. In addition, ASU 2016-10 categorizes intellectual property, or IP, into two categories: "functional" and "symbolic." Functional IP has significant standalone functionality. All other IP is considered symbolic IP. Revenue from licenses of functional IP is generally recognized at a point in time, while revenue from licenses of symbolic IP is recognized over time. ASU 2016-10 has the same effective date and transition requirements as ASU 2014-09, as amended by ASU 2015-14. In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606), Principal versus Agent Considerations (Reporting Revenue Gross versus Net)*, or ASU 2016-08, which clarifies the implementation guidance on principal versus agent considerations contained in ASU 2014-09 by specifying that the determination as to whether an entity that is involved in providing a good or a service to a customer is a principal or an agent is based upon whether the entity controls the good or the service before it is transferred to the customer. ASU 2016-08 has the same effective date and transition requirements as ASU 2014-09, as amended by ASU 2015-14. The adoption of ASU 2016-20 on January 1, 2018 did not have a material effect on the Company's financial position, results of operations or cash flows.

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers*, or ASU 2014-09, which provides a single, comprehensive revenue recognition model for all contracts with customers. The core principal of ASU 2014-09 is that an entity should recognize revenue when it transfers control of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. ASU 2014-09 is effective for annual periods, and interim periods within those annual periods,

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beginning after December 15, 2017 for public companies and December 15, 2018 for non-public companies. The Company is allowed to adopt ASU 2014-09 either (1) retrospectively to each prior reporting period presented using several practical expedients related to completed contracts and required disclosures, or (2) using a modified retrospective approach, with the cumulative effect of initially applying ASU 2014-09 recognized as an adjustment to the opening balance of retained earnings of the annual reporting period that includes the date of initial application, including disclosure of the effect of using this method of adoption on the financial statement line items. Because the Company has no contracts with customers, the adoption of ASU 2014-09 on January 1, 2018 did not have a material effect on the Company's financial position, results of operations or cash flows.

In November 2016, the Financial Accounting Standards Board, or FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230), Restricted Cash* (a consensus of the Emerging Issues Task Force), or ASU 2016-18, which changes the presentation of the cash flow statement to include amounts generally described as restricted cash or restricted cash equivalents, together with cash and cash equivalents, when reconciling the beginning-of-period and end-of-period amounts shown on the statement of cash flows. ASU 2016-18 also requires additional disclosures concerning the nature of the restrictions on cash and cash equivalents and a reconciliation between amounts of cash, cash equivalents and restricted cash on the balance sheet and statement of cash flows for each period presented. ASU 2016-18 was applied retrospectively to all periods presented and is effective for public business entities for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. Prior to adoption, the Company presented changes in restricted cash as an operating activity in the statement of cash flows. Upon adoption of ASU 2016-18 on January 1, 2018, such changes are now reflected in the beginning and ending balances of cash, cash equivalents and restricted cash for all periods presented. Cash flows used in operating activities decreased by \$441,049 and increased by \$321,468 for the years ended December 31, 2016 and 2017, respectively, and \$0 for the three month period ended March 31, 2017.

As of December 31, 2016, the Company adopted Accounting Standards Update, or ASU, 2014-15 *Presentation of Financial Statements – Going Concern (Subtopic 205-40), Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASU 2014-15, which is effective for annual periods ending after December 15, 2016, and interim periods within annual periods beginning after December 15, 2016. ASU 2014-15 codifies, for the first time within GAAP, management's responsibility to evaluate whether there is substantial doubt about the Company's ability to continue as a going concern and to provide related footnote disclosures in connection with preparing financial statements for each annual and interim reporting period. Substantial doubt about the Company's ability to continue as a going concern exists when there are conditions or events, considered in the aggregate, that are known and reasonably knowable at the date that the financial statements are issued, that indicate that the Company will be unable to meet its obligations as they become due within one year after that date. In that case, ASU 2014-15 requires the Company to disclose the nature of those conditions or events when they are present, management's plans to mitigate those conditions or events and whether or not such plans alleviated the substantial doubt. Management's evaluation as of the date of issuance of the consolidated financial statements for the year ended December 31, 2017 and three month period ended March 31, 2018 indicate that the Company will not be able to meet its obligations as they become due within one year of the financial statement issuance date (See Note 1).

As of January 1, 2016, the Company adopted ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting*, or ASU 2016-09, which amends Accounting Standards Codification, or ASC, *Topic 718, Compensation – Stock Compensation*, and is effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years for public companies and December 15, 2017 for non-public companies. The Company early adopted ASU 2016-09 during the year ended December 31, 2016. ASU 2016-09 simplifies several aspects of the accounting for share-based payment transactions, including the accounting for forfeitures, income tax consequences, classification of awards as either equity or liabilities, and

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classification on the statement of cash flows. The amendments will be applied prospectively. Upon adoption, the Company is accounting for forfeitures as they occur rather than estimate a forfeiture rate. As the Company did not issue any stock options prior to the date of adoption and the Company did not record any forfeitures related to restricted share grants to executives in 2015 as there was no expectation that they would leave the Company prior to the vesting dates, a cumulative-effect adjustment was not necessary. In periods subsequent to adoption, a higher expense is recognized earlier during the respective vesting periods of stock-based awards that are not forfeited. The income tax amendments within ASU 2016-09 will have no impact on its results of operations or cash flows because it is in a net operating loss position with a full valuation allowance.

*Recent Accounting Pronouncements Not Yet Adopted*

In December 2016, the FASB issued ASU No. 2016-20, *Technical Corrections and Improvements to Topic 606, Revenue from Contracts with Customers*, or ASU 2016-20, that allows entities not to disclose variable consideration allocated to performance obligations related to either: (1) sales— or usage -based royalties on licenses of intellectual property or (2) variable consideration allocated entirely to a wholly unsatisfied performance obligation or to a wholly unsatisfied promise to transfer a distinct good or service that forms part of a single performance obligation when certain criteria are met. ASU 2016-20 also requires entities that use any of the new or previously existing optional exemptions to expand their qualitative disclosures. It also makes 12 additional technical corrections and improvements to the new revenue standard, ASU 2014-09. The amendments have the same effective date and transition requirements as ASU 2014-09. The Company does not expect the adoption of ASU 2016-20 to have a material effect on its financial position, results of operations or cash flows.

In October 2016, the FASB issued ASU 2016-16, *Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other than Inventory*, or ASU 2016-16 which requires that an entity recognize the income tax consequences of an intra-entity transfer of assets other than inventory when the transfer occurs. The guidance must be applied using the modified retrospective basis. The Company does not expect the provisions of ASU 2016-16 to have a material impact on its current financial statements. This update will be effective for the Company at the beginning of fiscal 2019.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, or ASU 2016-02, which requires lessees to recognize the following for all leases (with the exception of short-term leases) at the commencement date: a lease liability, which is a lessee's obligation to make lease payments arising from a lease, measured on a discounted basis; and a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term. The revised guidance must be applied on a modified retrospective transition approach for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The revised guidance is effective for the Company at the beginning of Fiscal 2019. The Company is currently evaluating the impact this ASU will have on its consolidated financial statements.

**3. Asset Acquisition:**

Effective January 1, 2016, the Company and BRI-Alzan, Inc. ("BRI-Alzan"), a Delaware corporation, entered into an Agreement and Plan of Merger ("Agreement") to acquire all of the outstanding shares of BRI-Alzan from the shareholders of BRI-Alzan. Prior to entering into the Agreement, BRI-Alzan was an inactive entity that held a worldwide license agreement, dated May 1, 2013, with Brandeis University ("Brandeis") to develop certain pre-clinical technology for the treatment of ALS, but had not yet begun any development activities. In connection with the Agreement, the Company issued 300,000 Ordinary Shares and is required to make certain development milestone payments and royalty payments on the net sales of a product containing the technology in the event that the Company is able to achieve those milestones and develop a marketable product (see Note 14).

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The Company determined this transaction represented an asset acquisition as no processes were acquired as defined by ASC 805. The asset acquisition of in process research and development was recorded at a fair value of \$597,300 as of January 1, 2016. The acquired in process research and development was immediately charged to research and development expense in the statement of operations and comprehensive loss as of the acquisition date since the Company determined that there was no additional alternative use of these assets. Additionally, under ASC 805, the Company determined that as of the acquisition date and as of December 31, 2016, December 31, 2017 and March 31, 2018, the contingent milestone payments in the aggregate amount of \$4,500,000, and royalty payments have not been resolved and therefore have not been recorded as liability.

**4. Prepaid Expenses:**

Prepaid expenses for the periods presented consist of the following:

	December 31, 2016	December 31, 2017	March 31, 2018
Research and Development	\$ 418,483	\$ 624,348	\$ 630,196
Professional Fees	—	—	1,076,276
Clinical Trial Costs	204,028	497,869	503,941
Clinical Trial Materials	—	341,775	352,734
Dues and License Fees	49,487	145,594	106,012
Insurance	144,525	163,284	118,936
Rent	214,764	27,778	—
Other	180,896	160,595	28,318
	<u>\$ 1,212,183</u>	<u>\$ 1,961,243</u>	<u>\$ 2,816,413</u>

**5. Property & Equipment, net:**

Property and equipment, net for the periods presented consist of the following:

	December 31, 2016	December 31, 2017	March 31, 2018
Leasehold Improvements	\$ 2,203,282	\$ 10,873,895	\$ 11,284,844
Manufacturing Equipment	—	2,477,637	2,894,101
Laboratory Equipment	662,443	993,409	1,017,169
Office Equipment	100,350	276,100	282,172
Asset Retirement Obligation	205,659	153,133	158,044
Furniture & Fixtures	78,708	93,786	96,395
	<u>3,250,442</u>	<u>14,867,960</u>	<u>15,732,725</u>
Less: Accumulated depreciation	(233,917)	(612,231)	(1,089,634)
	<u>\$ 3,016,525</u>	<u>\$ 14,255,729</u>	<u>\$ 14,643,091</u>

In connection with an operating lease, the Company estimated that it had an asset retirement obligation, which is included in other liabilities on the consolidated balance sheets, at the end of the initial five-year lease term in the amount of \$306,400. The Company discounted the asset retirement obligation using an 8% discount rate and recorded an asset retirement obligation in the amount of \$205,659 as of December 31, 2016, which is included in leasehold improvements and was being depreciated over the five-year term of the lease (see Note 15). As of December 31, 2017, the Company determined that it is probable that it will exercise the additional five-year option provided for in the operating lease. Therefore, the company revalued the asset retirement obligation over the remaining eight-year lease term and recorded a reduction in the asset retirement obligation of \$75,011 recorded in leasehold improvements. The remaining net book value is being depreciated over the remaining eight-year lease term.

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Capitalized leases in the amount of \$17,817, \$95,880 and \$114,924 are included in office equipment at December 31, 2016 and 2017 and March 31, 2018, respectively, and accumulated depreciation of \$6,928, \$34,552 and \$46,390 at December 31, 2016 and 2017 and March 31, 2018, respectively.

Depreciation expense was \$243,081 and \$679,177 for the years ended December 31, 2016 and 2017, respectively and \$179,878 and \$458,836 for the three months ended March 31, 2017 and 2018, respectively.

**6. Restricted Cash:**

The Company is required to maintain stand-by letters of credit as security deposits under each of the ARE-East River Science Park LLC (“ARE”) leases (see Note 14). The fair value of each letter of credit approximates its contract value. In each case, the Company’s bank requires the Company to maintain restricted cash balances to serve as collateral for the letter of credit issued to the landlord by the bank. In connection with an amendment to one of the ARE leases in November 2017, the letter of credit in the amount of \$321,978 and the related restricted cash balance were released in December 2017. As of December 31, 2016 and 2017 and March 31, 2018, the restricted cash balances for the ARE leases were invested in a commercial money market account.

The restricted cash balance for the other ARE lease remains at \$123,376 through the end of the lease term in December 2021, plus three months.

The Company had \$444,844, \$123,376 and \$123,376 of restricted cash included in long-term assets as of December 31, 2016 and 2017 and March 31, 2018, respectively and is measured using level 1 inputs.

Upon the retrospective adoption of ASU 2016-18 on January 1, 2018, as discussed in Footnote 2, restricted cash is now reflected in the beginning and ending balance of cash, cash equivalents and restricted cash for all periods presented in the Consolidated Statements of Cash Flows. As a result of this retrospective adoption, cash flows used in operating activities decreased by \$441,049 and increased by \$321,468 for the years ended December 31, 2016 and 2017, and \$0 for the three month period ended March 31, 2017, respectively, resulting in revised net cash used in operating activities of \$14,367,952 and \$18,055,386 for the years ended December 31, 2016 and 2017, respectively, presented in the Consolidated Statements of Cash Flows.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the balance sheet that sum to the total of the same such amounts shown in the statement of cash flows:

	<u>December 31, 2016</u>	<u>December 31, 2017</u>	<u>March 31, 2018</u>
Cash and cash equivalents	\$ 17,476,641	\$ 8,548,638	\$ 32,356,851
Restricted cash	444,844	123,376	123,376
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	<u>\$ 17,921,485</u>	<u>\$ 8,672,014</u>	<u>\$ 32,480,227</u>

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**7. Accrued Expenses:**

Accrued expenses for the periods presented were comprised of the following:

	<u>December 31, 2016</u>	<u>December 31, 2017</u>	<u>March 31, 2018</u>
Clinical Trial Costs	\$ 664,149	\$ 4,859,410	\$ 4,243,611
Compensation and Benefits	1,418,958	2,386,903	390,896
Consulting	1,158,915	1,220,477	672,947
Rent	242,937	387,267	106,381
Professional Fees	323,102	231,923	910,081
Interest	—	33,437	25,500
Other	210,042	213,527	307,841
	<u>\$ 4,018,103</u>	<u>\$ 9,332,944</u>	<u>\$ 6,657,257</u>

**8. Capitalized Leases:**

In 2015, the Company acquired certain office equipment in the amount of \$17,817 under a 3-year lease arrangement. The Company determined that the lease should be capitalized since it contained a bargain purchase option for the equipment at the end of the lease term. Total payments under the capital lease amounted to \$20,502 and had an interest rate of 9.35%.

In 2017, the Company acquired additional office equipment in the amount of \$78,063 under a 3-year lease arrangement. The Company determined that the lease should be capitalized since it contained a bargain purchase option for the equipment at the end of the lease term. Total payments under the capital lease amounted to \$86,145 and had an interest rate of 6.90%.

The following is a schedule, by year, of future minimum lease payments under the capital leases together with the present value of the net minimum lease payments as of December 31, 2016 and 2017 and March 31, 2018:

	<u>December 31, 2016</u>	<u>December 31, 2017</u>	<u>March 31, 2018</u>
2018	\$ 6,834	\$ 34,410	\$ 25,523
2019	5,695	28,715	28,715
2020	—	7,179	7,179
Total minimum lease payments	12,529	70,304	61,417
Less: amount representing interest	(1,056)	(5,156)	(4,047)
Present value of net minimum lease payments	11,473	65,148	57,370
Less: current portion	(6,015)	(30,850)	(28,715)
Obligations under capital lease, less current portion	<u>\$ 5,458</u>	<u>\$ 34,298</u>	<u>\$ 28,655</u>

**9. Notes Payable**

On October 26, 2017, in connection with an amendment to an existing lease, the Company issued a promissory note in the amount of \$1,442,009 to ARE, the landlord and also a related party (see Note 14). The note bears interest at the rate of 5% per annum and is due on December 31, 2018. However, if the Company has



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sufficient liquidity, as defined in the note, then the note, including accrued interest, will become due and payable at that time. If the Company does not have sufficient liquidity, which is defined as Company's cash, cash equivalents and liquid short-term investments of at least an investment grade are at least twenty times greater than the promissory note plus accrued interest, the Company has the right to repay the note on the due date in either cash or Preferred Shares of the Company. In March 2018, the Company repaid the note in full in cash. The Company recorded interest expense in the consolidated statement of operations and comprehensive loss in connection with the note in the amount of \$13,037 and \$17,386 for the year ended December 31, 2017 and for the three months ended March 31, 2018, respectively.

**10. Share-Based Compensation**

***2016 Equity Incentive Plan***

The Company's 2016 Equity Incentive Plan (the "Plan"), was adopted by the Company's board of directors and shareholders. Under the Plan, the Company has granted share options to selected officers, employees and non-employee consultants. The Company's board of directors administer the Plan. Options granted under the Plan have a maximum contractual term of ten years. Options granted generally vest 25% on the first anniversary date of grant and the balance ratably over the next 36 months.

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A summary of the Company's share option activity related to employees, non-employee members of the board of directors and non-employee consultants as of and for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018 is as follows:

	<u>Number of Options</u>	<u>Weighted- Average Exercise Price</u>	<u>Aggregate Intrinsic Value</u>
Outstanding at December 31, 2015	—	\$ —	\$ —
Granted	1,295,000	1.99	
Exercised	—	—	
Expired	—	—	
Forfeited	—	—	
Outstanding at December 31, 2016	<u>1,295,000</u>	<u>\$ 1.99</u>	<u>\$ —</u>
Granted	2,375,000	0.96	
Exercised	(5,000)	(1.95)	
Expired	—	—	
Forfeited	(22,000)	(1.99)	
Outstanding at December 31, 2017	<u>3,643,000</u>	<u>\$ 1.32</u>	<u>\$ 1,420,650</u>
Granted	2,622,500	1.45	
Exercised	—	—	
Expired	—	—	
Forfeited	—	—	
Outstanding at March 31, 2018	<u>6,265,500</u>	<u>\$ 1.37</u>	<u>\$ 1,867,400</u>
Weighted average remaining contractual life of options outstanding as of December 31, 2016 (yrs)	<u>9.19</u>		
Weighted average remaining contractual life of options outstanding as of December 31, 2017 (yrs)	<u>9.09</u>		
Weighted average remaining contractual life of options outstanding as of March 31, 2018 (yrs)	<u>9.22</u>		
Options exercisable at December 31, 2016	<u>125,000</u>	<u>\$ 1.99</u>	<u>\$ —</u>
Options exercisable at December 31, 2017	<u>723,398</u>	<u>\$ 1.99</u>	<u>\$ —</u>
Options exercisable at March 31, 2018	<u>912,854</u>	<u>\$ 1.98</u>	<u>\$ —</u>
Weighted average remaining contractual life of options exercisable as of December 31, 2016 (yrs)	<u>9.24</u>		
Weighted average remaining contractual life of options exercisable as of December 31, 2017 (yrs)	<u>8.21</u>		
Weighted average remaining contractual life of options exercisable as of March 31, 2018 (yrs)	<u>8.07</u>		

The total fair value of options vested during the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018, was \$180,723, \$898,699 and \$309,147, respectively.

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During the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018, the Company granted 915,000, 1,020,000 and 2,070,000 share options, respectively, to employees and non-employee members of the board of directors. The grant date fair values of the stock options granted to those groups were estimated using the Black-Scholes option valuation model with the following ranges of assumptions (see Note 2):

	<u>For the Year Ended December 31,</u>		<u>For the Three Month</u>
	<u>2016</u>	<u>2017</u>	<u>Period Ended March 31,</u>
Risk-free interest rate	1.38% - 1.55%	2.28%	2.32% - 2.40%
Expected volatility	90%	90%	90%
Expected dividend yield	0%	0%	0%
Expected life of employee and Board of Directors' options (in years)	5.0 - 6.1	5.5 - 6.1	5.5 - 6.1

As of December 31, 2016 and 2017 and March 31, 2018, the total compensation expense relating to unvested options granted to employees and non-employee members of the board of directors that had not yet been recognized was \$800,976, \$987,413 and \$2,912,830, respectively which is expected to be realized over a period of 3.17, 3.42 and 3.78 years, respectively. The Company will issue shares upon exercise of options from Ordinary Shares reserved.

During the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018, the Company granted 380,000, 1,355,000 and 552,500 share options, respectively to non-employee consultants. In accordance with ASC 505-50, on December 31, 2016 and 2017 and March 31, 2018, the Company remeasured the fair value, of all unvested outstanding options that had been granted to non-employee consultants using the Black-Scholes option valuation model with the following ranges of assumptions:

	<u>For the Year Ended December 31,</u>		<u>For the Three Month</u>
	<u>2016</u>	<u>2017</u>	<u>Period Ended March 31,</u>
Risk-free interest rate	2.45%	2.36% - 2.39%	2.76% - 2.81%
Expected volatility	90%	90%	90%
Expected dividend yield	0%	0%	0%
Expected life of non-employee options (in years)	9.2 - 10.0	8.2 - 9.7	7.9 - 9.8

As of December 31, 2016 and 2017 and March 31, 2018, the total compensation expense relating to unvested options granted to non-employee consultants that had not yet been recognized was \$456,707, \$1,629,019 and \$2,130,007, respectively, which is expected to be realized over a period of 3.17, 3.72 and 3.78 years, respectively. The Company will issue shares upon exercise of options from Ordinary Shares reserved.

The weighted average grant date fair value of options granted to employees, non-employee members of the board of directors for their Board service and non-employee consultants during the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018 was \$1.51, \$0.80 and \$1.12, respectively.

### **Restricted Shares**

In 2015, in connection with certain service and consulting agreements, certain employees and a consultant were awarded an aggregate of 3,367,710 restricted Ordinary Shares and 750 restricted B ordinary shares, which restricted B ordinary shares were converted into restricted Ordinary Shares, of the Company. Such shares are subject to forfeiture over a three-year service period. The shares were valued at \$1.99 and \$2.00 per share and is included in loss from operations over the requisite service period.

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A summary of the restricted Ordinary Shares is as follows:

	<u>Ordinary Shares</u>	<u>\$ Value</u>
Total restricted Ordinary Shares Issued	3,368,460	\$ 6,730,290
Non-vested at December 31, 2015	2,590,478	5,175,857
Vested during 2016	1,090,049	2,155,666
Non-vested at December 31, 2016	1,500,429	3,020,191
Vested during 2017	1,089,380	2,154,330
Non-vested at December 31, 2017	411,049	865,861
Vested during the three-month period ended March 31, 2018	266,403	532,364
Non-vested at March 31, 2018	<u>144,646</u>	<u>\$ 333,497</u>

During the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018 the Company recognized total share-based compensation expense in the accompanying statements of operations and comprehensive loss as follows:

	<u>December 31, 2016</u>	<u>December 31, 2017</u>	<u>March 31, 2018</u>
Research and development	\$ 1,995,594	\$ 2,374,899	\$ 842,962
General and administrative	811,367	584,832	3,432,774
Total share based compensation	<u>2,806,961</u>	<u>\$ 2,959,731</u>	<u>\$ 4,275,736</u>

The Company does not expect to realize any tax benefits from its share option activity or the recognition of share-based compensation expense because the Company currently has net operating losses and has a full valuation allowance against its deferred tax assets. Accordingly, no amounts related to excess tax benefits have been reported in cash flows from operations or cash flows from financing activities for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018.

#### **11. Convertible Preferred C Shares and Shareholders' Deficit:**

##### ***Registration Rights Related to Ordinary Shares and Preferred Shares***

Holders of Preferred Shares who hold not less than 3% of the Company's fully diluted shares and certain other shareholders have piggyback registration rights with respect to the Company's registration of its Ordinary Shares following an initial public offering, subject to certain exceptions.

##### ***Drag-Along Rights Related to Ordinary and Preferred Shares***

Pursuant to the Company's articles of association, if the holders of at least 50% of the voting power of the Company wish to sell their Ordinary Shares and/or Preferred Shares, then such holders have the right to require all other holders to accept the offer made to them and sell their Ordinary Shares and/or Preferred Shares on the same terms, subject to certain exceptions with respect to the Company's registration of its Ordinary Shares.

##### ***Ordinary Shares***

###### *Voting Rights*

Each share is entitled to one vote.

###### *Redemption*

The shares are not redeemable.

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*Transfers*

Transfers to an affiliate or member, as defined, are permitted. Otherwise, the Ordinary Shares may not be transferred without approval from the Company's board of directors. If the transfer is approved, the Company has the right to purchase any or all of the Ordinary Shares on the same terms and conditions. If the Company does not exercise its right to purchase the Ordinary Shares, then the other shareholders have the right to purchase the Ordinary Shares on a pro-rata basis.

*Tag-Along Rights*

Pursuant to the Company's articles of association, if Kadmon holds more than 15% of the fully diluted share capital and proposes to transfer more than 25% of the aggregate number of Ordinary Shares held by Kadmon and its affiliates to a third-party purchaser, before making such a transfer Kadmon must offer to all of the MeiraGTx UK II founders the right to purchase the same proportion of the Ordinary Shares held by each MeiraGTx UK II founder on the proportion of shares being sold by Kadmon and its affiliates, subject to certain exceptions with respect to the Company's registration of its Ordinary Shares.

*Right to Appointment of Board Member*

Pursuant to the Company's shareholders' agreement, as long as Kadmon's ownership percentage of the Company is at least 10%, Kadmon has the right to appoint a board member to the Company's board of directors. This right in the shareholders' agreement terminates upon an initial public offering.

*Issuances*

*2016*

On January 1, 2016, the Company issued 300,000 Ordinary Shares in connection with the BRI-Alzan acquisition described in Note 3.

On April 5, 2016, the Company issued 4,017,048 Ordinary Shares in connection with the acquisition of the remaining 40% of MeiraGTx UK II described in Note 2.

On April 7, 2016, the Company issued 46,300 Ordinary Shares in connection with a consulting agreement.

On July 7, 2016, all of the 10,000 B ordinary shares outstanding were converted into 10,000 Ordinary Shares.

*2017*

On July 31, 2017, the Company issued 5,000 Ordinary Shares in connection with the exercise of an option.

On August 16, 2017, the Company issued 25,000 Ordinary Shares in connection with a research agreement.

*2018*

On March 1, 2018, a funding milestone was met under the employment agreements for certain senior management. Accordingly, the employees were issued an aggregate of 2,135,182 fully vested Ordinary Shares, which represented 3% of the fully-diluted outstanding shares of the Company as of such date. The shares were recorded as share-based compensation in the amount of \$3,096,104. Additionally, under the terms of the employment agreements, the Company was required to pay the income taxes on those shares on behalf of the

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executives. Total compensation expense in connection with the issuance of these Ordinary Shares, in the amount of \$6,154,608, was recorded as general and administrative expense during the three-month period ended March 31, 2018.

***Convertible Preferred C Shares***

*Redemption*

The Preferred Shares are not redeemable. However, in the event of a Sale (as defined in the Company's Articles of Association), which would include a change of control that is outside of the Company's control, the Preferred Shares are entitled to receive a payment which is equal to their liquidation value. The feature is being accounted for as a redemption under ASC 480.

The Company is accounting for its Preferred Shares under the requirements of ASC 480 which establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. The carrying value of the Preferred Shares is presented in as temporary equity and is increased by periodic accretions so that the carrying amount will equal the redemption amount at the estimated date that the Preferred Shares will be converted into Ordinary Shares. These increases are affected through charges against additional paid-in capital, to the extent it is available, or accumulated deficit. For all Preferred Shares issuances, the difference between the amount invested by the holders of the Preferred Shares, net of issuance costs, and the initial fair value of warrants issued in connection with the Preferred Shares (if applicable) and the liquidation value of the Preferred Shares, is recorded as accretion over the estimated life of the Preferred Shares. The accretion is added to net loss to arrive at the net loss available to Ordinary Shareholders in the calculation of loss per Ordinary Share.

*Liquidation Preference*

The Preferred Shares contain a liquidation preference whereby on a return of assets on liquidation or capital reduction or otherwise, the surplus assets and retained profits of the Company available for distribution among the holders of Shares shall be applied:

- first in paying to the holders of Preferred Shares a sum equal to \$2.70; and
- second, the balance of such assets (if any) shall be distributed amongst the holders of Ordinary Shares pro rata to the number of shares held by each of them respectively.

In September 2017, the shareholders amended the Company's articles of incorporation to reduce the liquidation value of the Preferred Shares from \$5.40 to \$2.70. Concurrently, the board of directors approved a dividend of 6,149,326 Preferred Shares to the existing holders of 6,149,326 Preferred Shares that had previously been purchased from the Company at a liquidation value of \$5.40 per share. The Company has accounted for this amendment as an extinguishment. The new Preferred Shares issued in connection with the extinguishment were recorded at fair value. The fair value of the newly issued Preferred Shares issued in connection with the extinguishment was determined based upon recent sales of the Company's Preferred Shares to third parties on or about the time of the extinguishment. The extinguishment and concurrent dividend resulted in \$0.1 million of loss being added to loss available to ordinary shareholders for earning per share purposes. (see Note 12).

*Conversion*

The Preferred Shares may be converted by the holder into Ordinary Shares, on a one to one basis, at any time, subject to adjustment for share splits and share dividends. The Preferred Shares shall automatically be converted and reclassified as Ordinary Shares with effect from and immediately prior to the completion of a Qualified IPO.

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*Dividends*

There are no dividends on the Preferred Shares.

*Voting Rights*

Each Preferred Share is entitled to one vote.

*Transfers*

Transfers to an affiliate or member, as defined, are permitted. Otherwise, the Preferred Shares may not be transferred without approval from the Company's board of directors. If the transfer is approved, the Company has the right to purchase any or all of the Preferred Shares on the same terms and conditions. If the Company does not exercise its right to purchase the Preferred Shares, then the other Preferred Shareholders has the right to purchase the Preferred Shares on a pro-rata basis.

*Pre-Emptive Rights*

The holders of the Preferred Shares have the right to participate in any new offering of equity shares in the same proportion as their holdings prior to the new offering.

*Tag-Along Rights*

If one or more of the holders proposes to transfer 15% or more of all shares issued by the Company, the transferee of the shares must offer to purchase from each holder of the Preferred Shares such proportion of the number of each class of shares registered in their name as is equal to the proportion which the shares that the transferor are proposing to transfer to the transferee.

*Right to Appointment of Board Member*

As long as Perceptive Life Sciences Master Fund, Ltd., holds not less than 50% of the Preferred Shares it owned on September 18, 2017 and April 12, 2018, it shall have the right to appoint a board member to the Company's board of directors, which it did on October 19, 2017. This right in the shareholders' agreement terminates upon an initial public offering.

*Issuances*

*2016*

During the year ended December 31, 2016, the Company issued 3,877,827 Preferred Shares at an offering price of \$5.40 per share for proceeds of \$20,770,031, net of issuance costs of \$177,623. The net proceeds of the offering are being used for working capital, research and development and general corporate purposes.

In April 2016, the Company issued 230,000 Preferred Shares in the amount of \$1,242,000 as partial payment for amounts due to Affiliate.

On December 20, 2016, the Company issued 59,259 Preferred Shares in connection with a license agreement described in Note 14.

*2017*

During the year ended December 31, 2017, the Company issued 37,800 Preferred Shares at an offering price of \$5.40 per share and 6,203,459 Preferred Shares at an offering price of \$2.70 per share for gross proceeds of \$16,854,656, excluding offering costs of \$98,804. The net proceeds of the offering are being used for working capital, research and development and general corporate purposes.

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On November 2, 2017, a note payable to a related party in the amount of \$2,500,000 was converted at the rate of \$2.70 per share, into 925,926 Preferred Shares (see Note 14).

2018

During the three-month period ended March 31, 2018, the Company issued 16,348,917 Preferred Shares at an offering price of \$2.70 per share for gross proceeds of \$44,142,076, excluding offering costs of \$290,475.

Also, during the three-month period ended March 31, 2018, the Company issued 501,886 Preferred Shares in lieu of cash payment of an aggregate amount \$1,355,097 to certain vendors.

On March 15, 2018, the Company issued 51,852 Preferred Shares in connection with a license agreement.

The net proceeds of the offering are being used for working capital, research and development and general corporate purposes.

**Warrants**

In connection with the issuance of 2,777,778 Preferred Shares on September 21, 2017, at an offering price of \$2.70 per share, the Company issued warrants to purchase 2,700,000 Preferred Shares at an exercise price of \$2.70 per share. The warrants expire on the first of the following to occur:

- (i) an Asset Sale;
- (ii) a Qualified IPO;
- (iii) a Share Sale;
- (iv) the winding up of the Company; or
- (v) On the third anniversary of the date of issuance

The Black-Scholes value of the warrants in the amount of \$1,660,500 was accounted for as a warrant liability and a discount to the Preferred Shares at the time of issuance and is being accreted over the expected term of the Preferred Shares (see Note 2).

In connection with the conversion of a \$2,500,000 note payable into 925,926 Preferred Shares on November 2, 2017, as an inducement to convert, the Company issued warrants to purchase 900,000 Preferred Shares to the note holder under the same terms and conditions as the warrants issued on September 21, 2017 (see Note 14).

The Black-Scholes value of the warrants in the amount of \$553,500 was recorded as a warrant liability and charged to convertible note inducement expense within the statement operations and comprehensive loss at the time of issuance.

Both of the warrants were revalued under the Black-Scholes valuation model at December 31, 2017 and March 31, 2018, which resulted in an increase of the warrant liability in the amount of \$465,633 and a decrease of the warrant liability in the amount of \$669,408, respectively, which was charged to change in fair value of warrant liability within the statement of operations and comprehensive loss.

The warrant liability at December 31, 2017 and March 31, 2018 was \$2,679,633 and \$2,010,225, respectively.



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**12. Net Loss per Share**

The Company computes net loss per share in accordance with ASC 260-10, *Earnings per Share* (see Note 2).

	<b>For the Year Ended December 31,</b>	
	<b>2016</b>	<b>2017</b>
Net loss attributable to MeiraGTX ordinary shareholders - basic and diluted	\$ (19,486,393)	\$ (31,044,535)
Accretion of Preferred Shares financing costs	(85,425)	(191,963)
Accretion of warrant	—	(615,000)
Adjusted net loss attributable to MeiraGTX ordinary shareholders - basic and diluted	<u>\$ (19,571,818)</u>	<u>\$ (31,851,498)</u>
Weighted-average ordinary shares outstanding:		
Basic and Diluted	31,098,591	33,269,157
Net loss per share:		
Basic and Diluted	<u>\$ (0.63)</u>	<u>\$ (0.96)</u>

	<b>For the Three Month Period Ended March 31,</b>	
	<b>2017</b>	<b>2018</b>
Net loss attributable to MeiraGTX ordinary shareholders - basic and diluted	\$ (6,820,385)	\$ (16,403,353)
Accretion of Preferred Shares financing costs	(22,761)	(94,445)
Accretion of warrant	—	(570,273)
Adjusted net loss attributable to MeiraGTX ordinary shareholders - basic and diluted	<u>\$ (6,843,146)</u>	<u>\$ (17,068,071)</u>
Weighted-average ordinary shares outstanding:		
Basic and Diluted	32,851,408	34,647,368
Net loss per share:		
Basic and Diluted	<u>\$ (0.21)</u>	<u>\$ (0.49)</u>

The following securities are considered to be Ordinary Share equivalents, but were not included in the computation of diluted net loss per Ordinary Share because to do so would have been anti-dilutive:

	<u>December 31, 2016</u>	<u>December 31, 2017</u>
Preferred Shares	6,111,256	19,428,037
A restricted ordinary shares subject to forfeiture	1,489,333	411,049
Stock options	1,295,000	3,643,000
Warrants	—	3,600,000
	<u>8,895,589</u>	<u>27,082,086</u>

	<u>March 31, 2017</u>	<u>March 31, 2018</u>
Preferred Shares	6,149,326	36,330,692
A restricted ordinary shares subject to forfeiture	1,222,930	144,646
Stock options	1,720,000	6,265,500
Warrants	—	3,600,000
	<u>9,092,256</u>	<u>46,340,838</u>

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**13. Income Taxes:**

Since the Company has recurring losses and a valuation allowance against deferred tax assets, there is no tax expense (benefit) for the years ended December 31, 2016 or 2017 and for the three month periods ended March 31, 2017 or 2018.

Each Company files separate tax returns in its respective tax jurisdictions.

As of December 31, 2017, the Company had federal and state net operating loss (“NOL”) carryforwards in the United States of approximately \$7,820,000 and \$7,779,000, respectively, and in the United Kingdom of approximately \$39,971,000, which are available to reduce future taxable income. The U.S. federal and state NOL carry forwards will begin to expire in 2035 and the U.K. NOL will continue indefinitely under current UK legislation. Also, as of December 31, 2017, the Company had research and development credits in the U.S. in the amount of \$697,000. The NOL carry forwards are subject to review and possible adjustment by the U.S., U.K. and state tax authorities. NOL carry forwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders, as defined under Sections 382 Internal Revenue Code, as well as CTA 2010 Part 14 under the UK tax rules. This could limit the amount of NOLs that the Company can utilize annually to offset future taxable income or tax liabilities. As of December 31, 2017, the Company has not performed such an analysis. Subsequent ownership changes and proposed future changes to the UK (or US) tax rules in respect of the utilization of losses carried forward may further affect the limitation in future years. Additionally, the Company has not undertaken a study on the completeness of the U.S. research and development credit. As such, the U.S. research and development credits may change.

The Company’s pre tax earnings from the United Kingdom and United States locations are as follows:

	<b>December 31, 2016</b>	<b>December 31, 2017</b>
United Kingdom	\$ (17,285,861)	\$ (26,458,625)
United States	(2,506,415)	(4,585,910)
	<u>\$ (19,792,276)</u>	<u>\$ (31,044,535)</u>

The Company is subject to the corporate tax rate in the U.K. as a Limited U.K. corporation.

The following table summarizes a reconciliation of income tax benefit compared with the amounts at the U.K. statutory income tax rate:

	<b>December 31, 2016</b>		<b>December 31, 2017</b>	
Statutory rate	(3,958,455)	20.00%	(5,976,073)	19.25%
U.K. R&D credit	—	0.00%	654,648	-2.11%
Permanent differences—other	680,255	-3.44%	539,136	-1.74%
Impact of foreign exchange	—	0.00%	(152,948)	0.49%
U.S. R&D credit	(238,850)	1.21%	(363,665)	1.17%
Foreign tax rate differential	(341,603)	1.73%	(673,619)	2.17%
State and local rate, net of federal tax	(240,465)	1.21%	(446,683)	1.44%
Future UK Rate Change (17% at expected DTA turn)	582,910	-2.95%	482,351	-1.55%
Federal & State Rate Change (Jobs Act & MTA)	—	0.00%	993,998	-3.20%
Change in valuation allowance	<u>3,516,208</u>	<u>-17.77%</u>	<u>4,942,855</u>	<u>-15.92%</u>
Actual income tax benefit effective tax rate	<u>—</u>	<u>0.00%</u>	<u>—</u>	<u>0.00%</u>

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The Expense/(Benefit) for income taxes from continuing operations consists of the following:

	<u>December 31, 2016</u>	<u>December 31, 2017</u>
<b>Current Tax Expense/(Benefit)</b>		
United Kingdom	—	—
United States	—	—
Total Current	<u>—</u>	<u>—</u>
<b>Deferred Tax Expense/(Benefit)</b>		
United Kingdom	(2,034,368)	(3,759,109)
United States	(1,481,840)	(1,183,746)
Total Deferred	<u>(3,516,208)</u>	<u>(4,942,855)</u>
Change in Valuation Allowance	3,516,208	4,942,855
Total Income Tax Expense/(Benefit)	<u>—</u>	<u>—</u>

**Deferred Tax Assets/(Liabilities)**

	<u>Total</u>	<u>December 31, 2016</u>	
		<u>UK</u>	<u>US</u>
<b>Deferred Tax Assets:</b>			
Net operating loss carryforwards	\$ 5,048,704	\$ 3,176,927	\$ 1,871,777
Other	373,805	126,232	247,573
R&D Credit	333,741	—	333,741
Deferred tax assets	<u>5,756,250</u>	<u>3,303,159</u>	<u>2,453,091</u>
Less: valuation allowance	<u>(5,756,250)</u>	<u>(3,303,159)</u>	<u>(2,453,091)</u>
Net deferred tax asset	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>

	<u>Total</u>	<u>December 31, 2017</u>	
		<u>UK</u>	<u>US</u>
<b>Deferred Tax Assets:</b>			
Net operating loss carryforwards	\$ 9,462,690	\$ 6,909,754	\$ 2,552,937
Other	539,008	152,554	386,454
R&D Credit	697,406	—	697,406
Deferred tax assets	<u>10,699,105</u>	<u>7,062,308</u>	<u>3,636,797</u>
Less: valuation allowance	<u>(10,699,105)</u>	<u>(7,062,308)</u>	<u>(3,636,797)</u>
Net deferred tax asset	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of available evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a full valuation allowance against its deferred tax assets at December 31, 2016 and 2017 because the Company's management has determined that it is more likely than not that these assets will not be fully realized.

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Changes to the U.K. and U.S. corporation tax rates have been announced which will impact future accounting periods. In his budget of July 8, 2015, the Chancellor of the Exchequer announced a reduction in the U.K. corporation tax rate to 19% for the financial year beginning April 1, 2017 and a further reduction to 18% for the financial year beginning April 1, 2020. These changes received Royal Assent on November 18, 2015. The U.K. Finance Act 2016 provides for a further reduction in the corporation tax rate to 17% for the Financial Year beginning April 1, 2020. This change was enacted on September 15, 2016. As the Company does not expect to be able to utilize its NOL's in the U.K. prior to its financial year beginning on January 1, 2021, if at all, the deferred tax has been calculated using a tax rate of 17%.

In the United States, the corporation tax rate was reduced to 21% for the financial year beginning January 1, 2018. As these changes were enacted prior to the December 31, 2017 balance sheet date, deferred tax has been calculated accordingly in these consolidated financial statements, which represented a decrease in the prior years deferred tax assets of approximately \$994,000.

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2016 and 2017, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations and comprehensive loss.

The Company files income tax returns in the United States and the United Kingdom, and various state jurisdictions. For tax years 2015, 2016 and 2017, the statute of examination is open in all jurisdictions in which the Company files income tax returns. The Company does not have any earnings, therefore no provision has been made for income taxes that would be payable against such foreign earnings.

#### **14. Related Party Transactions:**

##### ***Transition Services Agreement***

Effective April 24, 2015, the Company entered into a transition services agreement (the "TSA") with Kadmon, whereby Kadmon would provide office and laboratory facilities as well as certain other personnel support activities to the Company. Under the agreement, the Company is charged for (i) rent based upon the square footage of the office and laboratory facilities used by the Company (ii) other personnel support activities based upon the hours of the personnel providing the support activities, and (iii) and other direct costs incurred by Kadmon on behalf of the Company, plus a 7% administrative fee. The TSA may be terminated by either party by giving thirty-days' notice.

During the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, the Company incurred the following charges in connection with the TSA and is included in loss from operations:

	Years Ended December 31,		Three Months Ended March 31,	
	2016	2017	2017	2018
Rent	\$ 794,087	\$548,229	\$ 123,355	\$ 136,353
Personnel	189,104	39,721	18,532	6,493
Other	42,110	5,983	5,080	—
Total charges incurred	<u>\$1,025,301</u>	<u>\$593,933</u>	<u>\$ 146,967</u>	<u>\$ 142,846</u>

During the year ended December 31, 2016 and 2017, the Company made cash payments totaling \$225,078 and \$275,941, respectively. During the three-month periods ended March 31, 2017 and 2018, the

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Company made cash payments totaling \$275,941 and \$997,417, respectively. Additionally, in April 2016, as partial payment of the amounts owed to Kadmon, the Company issued 230,000 Preferred Shares in the amount of \$1,242,000.

The amount due to Kadmon at December 31, 2016 and 2017 and March 31, 2018, is \$543,038, \$861,030, and \$6,493, respectively and is disclosed as Due to Kadmon on the balance sheet.

***Research Agreement***

Effective October 23, 2016, the Company entered into a four-year master services agreement with UCL Consultants Limited, an entity affiliated with University College of London (“UCL”), which is a shareholder of the Company. Pursuant to the agreement, UCL Consultants Limited provides pre-clinical research and development under the direction of the Company. In connection with the agreement, the Company issued several work orders during the years ended December 31, 2016 and 2017 in the aggregate amounts of £1,161,149 and £241,053, respectively, or approximately \$1,574,000 and \$311,000, based upon the average exchange rates during the years ended December 31, 2016 and 2017, respectively. Either party may terminate the agreement by giving 30 days written notice. Total research and development expenses under this agreement for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018 was approximately \$278,000 and \$538,000, and \$108,000 and \$189,000, respectively. Future obligations, under the agreement equal £927,823, or approximately \$1,301,921 through October 2020.

The amount due to UCL under the master services agreement at December 31, 2016 and 2017 and March 31, 2018, is \$251,754, \$775,315 and \$377,145, respectively and is included in accounts payable and accrued expenses on the balance sheet.

***Manufacturing Agreement***

Effective September 1, 2016, the Company entered into a manufacturing and drug supply agreement with UCL. Pursuant to the agreement, UCL will manufacture materials for the Company’s clinical trials under the direction of the Company. Either party may terminate the agreement by giving 30 days written notice. The agreement was terminated in January 2018. Total research and development expenses under this agreement for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, was approximately \$456,106 and \$1,904,352, and \$563,024 and \$0, respectively.

The amount due to UCL under the manufacturing and drug supply agreement at December 31, 2016 and 2017 and March 31, 2018, is \$412,395, \$2,466,142 and \$2,545,226, respectively and is included in accrued expenses on the balance sheet.

***Leases***

*July 2016 Lease*

Effective July 1, 2016, the Company entered into a non-cancellable operating lease for laboratory and related office facilities in New York with ARE, an entity that is under common control by an entity that is a minority shareholder of the Company and whose CEO is a director of the Company. The lease provides for monthly base rent and property management fees, including rent escalations and rent holidays, plus operating expenses during the lease term, which expires on December 31, 2021. The Company records monthly rent expense on a straight-line basis from July 1, 2016 through December 31, 2021. As of December 31, 2016 and 2017 and March 31, 2018, the balance of deferred rent, representing the difference between cash rent paid and straight-line rent expense, was \$243,780, \$231,276 and \$225,999, respectively.

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Total rent expense under this operating lease was \$243,780 and \$487,559 for the years ended December 31, 2016 and 2017, respectively, and \$121,890 for the three months ended March 31, 2017 and 2018. As of March 31, 2018, the aggregate future minimum rental payments under this lease are \$2,054,343.

In connection with the signing of this lease, the Company entered into a standby letter of credit agreement for \$122,866, which serves as a security deposit for the premises. The standby letter of credit expires on July 7, 2017 and is automatically renewed annually through July 7, 2021. This standby letter of credit is secured with restricted cash in a money market account (see Note 6).

*December 2016 Lease*

Effective December 15, 2016, the Company entered into another non-cancellable operating lease with ARE, expiring on October 31, 2032, for laboratory and office facilities in New York. The lease provided for monthly base rent, including rent escalations, property management fees and rent holidays, plus operating expenses during the lease term. The Company recorded monthly rent expense on a straight-line basis from December 15, 2016 through October 31, 2032. On October 26, 2017, the lease was amended, whereby the lease would terminate on March 31, 2018 and only base rent and management fees in the aggregate amount of \$563,507 would be due from November 1, 2017 through March 31, 2018. Under the amendment, the Company issued a note to ARE in the amount of \$1,442,009 (see Note 9), removed the balance of the deferred rent and accrued the future rent payments, all of which were recorded as rent expense at the time of the amendment, in accordance with ASC 420, Exit and Disposal Activities, as the Company had a cease use date as of the date of the amendment. As of December 31, 2016 and 2017 and March 31, 2018, the balance of deferred lease obligation, representing the difference between cash rent paid and straight-line rent expense, was \$11,380, \$0 and \$0, respectively.

Total rent expense under this operating lease was \$43,578 and \$1,660,806 for the years ended December 31, 2016 and 2017, and \$390,903 and \$0 for the three months ended March 31, 2017 and 2018, respectively.

On October 26, 2017, in connection with the amendment to the lease, the Company issued a promissory note in the amount of \$1,442,009 to ARE. The note accrued interest at the rate of 5% per annum and was due on December 31, 2018. However, if the Company had sufficient liquidity, as defined in the note, then the note, including accrued interest, would become due and payable at that time. In accordance with the sufficient liquidity provision, the Company repaid the note, plus accrued interest, in the aggregate amount of \$1,472,433 during the three-month period ended March 31, 2018.

The Company recorded interest expense in the consolidated statement of operations and comprehensive loss in connection with the note in the amount of \$17,387 for the three-month period ended March 31, 2018.

***Convertible Note Payable***

On May 1, 2017, the Company issued a convertible note in the amount of \$2,500,000 to ARE. The note had an interest at a rate of 10% per annum and was convertible into Preferred Shares at any time at the option of the holder or would automatically convert into Preferred Shares in the event of an equity investment by a mutually agreed upon institutional investor at a price per share equal to the lowest price paid per share by a purchaser of the Company's Preferred Shares. On November 2, 2017 the note was converted to 925,926 Preferred Shares at \$2.70 per share. In accordance with the terms of the convertible note, the accrued interest in the amount of \$145,833 was cancelled.

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As an inducement to convert the convertible note, the Company issued a warrant to purchase 900,000 Preferred Shares, at an exercise price of \$2.70 per share, to the holder of the convertible note, which was expenses in accordance with ASC 470 (see Note 11).

**15. Commitments:**

***Operating Leases***

In February 2016, the Company entered into a non-cancellable operating lease, expiring in February 2021, for manufacturing and office facilities in London, UK. The lease provides for an additional five-year term at the Company's option. The lease provides for monthly base rent, plus operating expenses and real estate taxes during the lease term.

In connection with a provision in the lease requiring the Company to remove all equipment and leasehold improvements upon the termination of the lease, the Company estimated that it had an asset retirement obligation at the end of the lease term in the amount of \$306,400. The Company discounted the asset retirement obligation using an 8% discount rate and recorded an asset retirement obligation in the amount of \$205,659, which is included in leasehold improvements. As of December 31, 2017, the Company determined that it will more likely than not exercise the additional five-year option provided for in the operating lease. Therefore, the company revalued the asset retirement obligation over the remaining eight-year lease term and recorded a reduction in the asset retirement obligation of \$75,011. During the years ended December 31, 2016 and 2017, and the three months ended March 31, 2017 and 2018, the Company recorded \$17,247 and \$7,571 and \$4,685 and \$3,678 of interest expense, respectively. The carrying value of the asset retirement obligation at December 31, 2016 and 2017 and March 31, 2018 is \$221,254, \$178,419 and \$187,848, respectively. Total rent expense under this operating lease was \$266,698 and \$279,303 for the years ended December 31, 2016 and 2017, respectively, and \$67,259 and \$74,001 for the three months ended March 31, 2017 and 2018, respectively.

On October 1, 2017, the Company entered into a one-year non-cancellable operating lease, expiring in September 2018, for office and laboratory facilities in Leiden, Netherlands. The lease provides for monthly base rent plus operating expenses during the lease term. The lease provides for successive one-year extensions up to a maximum of four extensions. Total rent expense under this operating lease was \$0 and \$5,273 for the years ended December 31, 2016 and 2017, respectively, and \$0 and \$2,703 for the three months ended March 31, 2017 and 2018, respectively.

In June 2017, the Company entered into two non-cancellable operating leases, expiring in July 2018, for office facilities in London, UK. The lease provides for monthly base rent, rent holidays plus operating expenses and real estate taxes during the lease term. The Company records monthly rent expense on a straight-line basis from June 1, 2017 through July 23, 2018. As of December 31, 2017 and March 31, 2018, the balance of deferred lease obligation, representing the difference between cash rent paid and straight-line rent expense, was \$35,014 and \$15,489, respectively. Total rent expense under these operating leases was \$0 and \$85,222 for the years ended December 31, 2016 and 2017, respectively, and \$0 and \$27,774 for the three months ended March 31, 2017 and 2018, respectively.

The aggregate future minimum rental payments under these leases as of December 31, 2017 are as follows:

2018	\$365,713
2019	\$293,130
2020	\$293,130
2021	\$ 24,427
Total future rent payments	<u>\$976,400</u>

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The aggregate future minimum rental payments of all leases, including those discussed in Note 14, as of December 31, 2017 are as follows:

2018	\$1,215,723
2019	\$ 828,813
2020	\$ 847,562
2021	\$ 598,264
Total future rent payments	<u>\$3,490,362</u>

### ***Service Agreements***

On April 27, 2015, the Company entered into service agreements with a senior officer and a greater than 5% shareholder of the Company. Under the terms of the agreements, the employees will receive aggregate compensation of £300,000 per annum, or approximately \$408,000 using exchange rates as of December 31, 2017. The agreements also provide for contributions to a defined contribution pension plan to be set up by the Company and a discretionary bonus. The agreements may be terminated at any time by either party by giving twelve-months' notice, or the Company may terminate the officer's employment effective immediately upon notice, and within 28 days making payment in lieu of notice consisting of a sum equivalent to the officer's annual salary for the relevant period. For the years ended December 31, 2016 and 2017, the Company recorded £430,000 and £724,000 or approximately \$583,000 and \$933,000, respectively, using the average exchange rates during the year ended December 31, 2016 and 2017, respectively, in research and development costs under these agreements. For the three months ended March 31, 2017 and 2018, the Company recorded £83,000 and £103,000 or approximately \$102,000 and \$145,000, respectively, using the average exchange rates during the three months ended March 31, 2017 and 2018, respectively, in research and development costs under these agreements. Future obligations to be paid under these agreements equal £34,000, or approximately \$48,000, using exchange rates as of March 31, 2018.

In connection with the service agreements, on April 24, 2015, the employees were awarded, under a share award agreement, an aggregate of 2,704,800 restricted Ordinary Shares and 750 B ordinary shares, which B ordinary shares have been converted into Ordinary Shares of the Company. Under the Share Award Agreement, such shares are subject to forfeiture ratably over a period of three years if the employee's do not remain an employee or consultant to the Company. The shares were valued at \$2.00 per share and, in accordance with ASC718, are being charged to operations as stock compensation ratably over the forfeiture period.

### ***Employment Agreements***

In February 2016, the Company entered into three-year employment agreements with certain senior officers of the Company. Under the terms of the agreements, the employees will receive annual compensation in the aggregate amount of \$710,000, which was increased to a maximum aggregate amount of \$1,075,000. The employment agreements also provide for an annual guaranteed cash bonus targeted at 100% of annual compensation. The agreements also provide for discretionary annual performance bonuses targeted to be not less than 50-60% of the employee's base salary and grants of restricted stock. In January 2018 the Company's compensation committee approved a discretionary bonus in the aggregate amount of \$1,196,000. This discretionary bonus and the guaranteed bonus for 2017, in the amount of \$850,000, are subject to compensation committee approval and meeting certain future funding conditions. On February 28, 2018, the funding conditions were met.



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Additionally, the agreements provide for equity incentives of up to an aggregate a maximum of 8.0% of the Company's fully diluted outstanding shares upon the attainment of certain milestones. On March 1, 2018, a funding milestone was met. Accordingly, the employees were issued an aggregate of 3% of the fully-diluted outstanding shares of the Company as of such date. (see Note 17).

The employees are also entitled to participate in all incentive and deferred compensation and employee benefit programs available to employees and executive officers of the Company. Future obligations to be paid under these agreements equal \$1,881,250, as of March 31, 2018.

***Consulting and other Agreements***

Effective September 28, 2015, the Company entered into a three-year consulting agreement with a consultant to provide ongoing strategic advice and to serve on the Company's board of directors. In connection with the agreement, the Company issued 662,910 restricted Ordinary Shares. Under the consulting agreement, such shares are subject to forfeiture ratably over a period of three years if the consultant does not remain a consultant to the Company. The shares were valued at \$1.99 per share and are being charged to general and administrative expenses upon the expiration of each forfeiture period.

***Research Agreements***

On April 24, 2015, the Company entered into a cooperative research and development agreement (CRADA) with the U.S. Department of Health & Human Services, as represented by the National Institute of Dental and Craniofacial Research (NIDCR) and Institute or Center of the National Institutes of Health (NIH). The CRADA provided for quarterly payments of \$21,250 for three years through April 30, 2017 and a cost per patient for each patient enrolled in the Company's xerostomia clinical trial. The CRADA was amended on March 25, 2016 to extend the term through March 25, 2021 and to extend the annual payments throughout the revised term. Research and development expenses under the CRADA for the year ended December 31, 2016 and 2017 were \$76,161 and \$115,374, respectively, and for the three months ended March 31, 2017 and 2018 were \$25,002 and \$28,348, respectively. Future obligations to be paid under the CRADA, as amended, through March 25, 2021 equal \$255,000.

On March 22, 2016, the Company entered into a five-year cooperative research and development agreement (CRADA) with the U.S. Department of Health & Human Services, as represented by the National Institute of Dental and Craniofacial Research (NIDCR) and Institute or Center of the National Institutes of Health (NIH) for the treatment of Sjogren's Syndrome associated salivary hypofunction. The CRADA provides for quarterly payments of \$104,500 for the first three years of the agreement plus a cost per patient for each patient enrolled in a clinical trial. The costs associated with years four and five of the CRADA will be determined at a later date. Total research and development expenses under this agreement for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, were \$325,343, \$418,000, \$104,500 and \$104,500, respectively. Future obligations to be paid under the agreement through March 22, 2019 equal \$313,500.

Effective December 5, 2016, the Company entered into a three-year research collaboration agreement with Cornell University. Pursuant to the agreement, Cornell University provides research and development under the direction of the Company. In connection with the agreement, in July 2017, the Company issued 25,000 Ordinary Shares to Cornell University, which were recorded as research and development expenses in the amount of \$17,000. The Company amended this agreement effective June 12, 2017 to add a second three-year research collaboration project through September 2019. Total research and development expenses under this agreement, as amended, for the years ended December 31, 2016 and 2017 and for the three months ended March 31, 2017 and 2018, were \$63,337 and \$1,029,904, and \$190,011 and \$448,173, respectively. Future obligations to be paid under the agreement through December 5, 2019 equal \$2,898,602.

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On February 14, 2017, the Company entered into a one-year research collaboration agreement with Cornell University in the amount of \$679,473. On August 24, 2017, the agreement was amended to add an additional study in the amount of \$182,520. Total research and development expenses under this agreement for the years ended December 31, 2016 and 2017 and for the three months ended March 31, 2017 and 2018, were \$0 and \$698,307, and \$91,401 and \$77,177, respectively.

***License Agreements***

Effective February 4, 2015, the Company entered into an exclusive worldwide license agreement with UCL Business, PLC (“UCL Business”), an entity that employs the Company’s Chief Scientific Officer, to develop up to eight programs using certain ocular gene therapy technology. Under the terms of the agreement, as amended, the Company will pay UCL Business certain sales milestone payments, if achieved, in the aggregate amount of £39.8 million, or approximately \$54.0 million using the exchange rate at December 31, 2017, and royalties on net sales, as defined upon commercialization. Additionally, the Company is responsible for all patent prosecution and maintenance costs incurred and will also pay UCL Business an annual maintenance fee of £50,000, or approximately \$68,000, until the first commercial sale of a product. The agreement will terminate upon the later of (i) the last valid claim in a relevant product (ii) the expiration of regulatory exclusivity to all licensed products, or (iii) the 10<sup>th</sup> anniversary of the first commercial sale of a product. Total research and development expenses under the agreement for the years ended December 31, 2016 and 2017, and the three months ended March 31, 2017 and 2018, were \$67,775 and \$73,250, and \$61,996 and \$79,738, respectively.

On July 28, 2017, the Company entered into another worldwide license agreement with UCL Business for an additional program using certain ocular gene therapy technology. The Company will pay UCL Business certain milestone payments, royalties and annual maintenance fees under the same terms and conditions as the license dated February 4, 2015. Total research and development expenses under the agreement for the years ended December 31, 2016 and 2017, and the three months ended March 31, 2017 and 2018, were \$0, \$82,260 and \$0, respectively.

Effective March 15, 2018, the Company entered into a third exclusive worldwide license agreement with UCL Business for an additional program using certain ocular gene therapy technology. The Company issued 51,852 Preferred Shares to UCL Business, which were recorded as research and development expenses in the amount of \$140,000 during the three-month period ended March 31, 2018, and will pay UCL Business certain milestone payments, royalties and annual maintenance fees under the same terms and conditions as the license dated February 4, 2015. The Company did not incur any additional research and development expenses under the agreement during the three-month period ended March 31, 2018.

Effective January 1, 2016, the Company entered into an Agreement (“Agreement”) and Plan of Merger to acquire all of the outstanding shares of BRI-Alzan from the shareholders of BRI-Alzan. In connection with the Agreement, the Company will pay certain development milestone payments if achieved, in the aggregate amount of \$4.5 million, and annual royalty payments on annual net sales following the first commercial sale of any product containing the technology acquired (see Note 3).

**16. Employee Benefit Plans**

***United States***

During the year ended December 31, 2016, Meira LLC participated in the Kadmon 401K Plan. On January 1, 2017, Meira LLC adopted its own defined contribution retirement plan that complies with Section 401(k) of the Internal Revenue Code. All Meira LLC employees over the age of 21 are eligible to participate in the plan after three consecutive months of service. Employees are able to defer a portion of their pay into the plan on the first day of the month on or after the day all age and service requirements have been met.

**MEIRAGTX LIMITED AND SUBSIDIARIES**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

The plan provides for a Company matching contribution. All eligible employees receive an employer matching contribution equal to the lesser of the amount the employee contributes to the plan or 6% of their salary up to the annual IRS limit.

***United Kingdom***

On August 1, 2016, MeiraGTx UK II adopted a defined contribution group personal pension plan that complies with HM Revenue and Customs (HMRC) for tax relief. All MeiraGTx UK II employees are eligible to participate in the plan upon joining service. All eligible employees, if they elect to join the pension scheme, receive an employer pension contribution equal to 7.5% to 10.0% of their pensionable earnings. Currently, employees are not required to contribute, but may make optional contributions up to the annual allowance HMRC limits.

Under the HMRC requirements, current required minimum employer contributions are 2-3% but will rise to between 5-6% after April 2018 and 8-9% after April 2019.

During the years ended December 31, 2016 and 2017, and three months ended March 31, 2017 and 2018, employer contributions to all plans were \$128,281, \$252,700, \$73,838 and \$147,566, respectively.

**17. Subsequent Events:**

Management has evaluated subsequent events through the date of this filing. Based on our evaluation, the following disclosures have been made:

***Preferred Shares***

From April 1, 2018 through April 30, 2018, the Company issued 4,706,495 Preferred Shares at an offering price of \$2.70 per share for gross proceeds in the amount of \$12,707,536.

Through and including \_\_\_\_\_, 2018 (the 25th day after the date of this prospectus), all dealers effecting transactions in the ordinary shares, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

## Shares



### Ordinary Shares

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#### PROSPECTUS

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**BofA Merrill Lynch**

**Barclays**

**Evercore ISI**

**Chardan**

, 2018

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**Part II****INFORMATION NOT REQUIRED IN PROSPECTUS****Item 13. Other Expenses of Issuance and Distribution.**

The following table indicates the expenses to be incurred in connection with the offering described in this registration statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimated except the Securities and Exchange Commission registration fee, the Financial Industry Regulatory Authority, Inc., or FINRA, filing fee and the Nasdaq listing fee.

	<u>Amount</u>
Securities and Exchange Commission registration fee	\$ *
FINRA filing fee	*
Initial listing fee	*
Accountants' fees and expenses	*
Legal fees and expenses	*
Blue Sky fees and expenses	*
Transfer Agent's fees and expenses	*
Printing and engraving expenses	*
Miscellaneous	*
Total expenses	<u>\$ *</u>

\* To be filed by amendment.

**Item 14. Indemnification of Directors and Officers.**

Cayman Islands law does not limit the extent to which a company's amended and restated memorandum and articles of association may provide for indemnification of officers and directors, except to the extent any such provision may be held by the Cayman Islands courts to be contrary to public policy, such as to provide indemnification against civil fraud or the consequences of committing a crime. Our amended and restated memorandum and articles of association, which will become effective upon the completion of this offering, provide that our board of directors and officers shall be indemnified from and against all liability which they incur in execution of their duty in their respective offices, except liability incurred by reason of such directors' or officers' dishonesty, willful default or fraud.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is theretofore unenforceable.

Our amended and restated memorandum and articles of association will provide:

"Every Director (including for the purposes of this Article any alternate Director appointed pursuant to the provisions of these Articles), Secretary, assistant Secretary, or other Officer (but not including the Company's auditors) and the personal representatives of the same (each an "Indemnified Person") shall be indemnified and secured harmless against all actions, proceedings, costs, charges, expenses, losses, damages or liabilities incurred or sustained by such Indemnified Person, other than by reason of such Indemnified Person's own dishonesty, willful default or fraud as determined by a court of competent jurisdiction, in or about the conduct of the Company's business or affairs (including as a result of any mistake of judgment) or in the execution or discharge of his duties, powers, authorities or discretions, including without prejudice to the generality of the foregoing,

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any costs, expenses, losses or liabilities incurred by such Indemnified Person in defending (whether successfully or otherwise) any civil proceedings concerning the Company or its affairs in any court whether in the Cayman Islands or elsewhere.

139. No Indemnified Person shall be liable:

(a) for the acts, receipts, neglects, defaults or omissions of any other Director or Officer or agent of the Company; or

(b) for any loss on account of defect of title to any property of the Company; or

(c) on account of the insufficiency of any security in or upon which any money of the Company shall be invested; or

(d) for any loss incurred through any bank, broker or other similar Person; or

(e) for any loss occasioned by any negligence, default, breach of duty, breach of trust, error of judgement or oversight on such Indemnified Person's part; or

(f) for any loss, damage or misfortune whatsoever which may happen in or arise from the execution or discharge of the duties, powers, authorities, or discretions of such Indemnified Person's office or in relation thereto;

unless the same shall happen through such Indemnified Person's own dishonesty, willful default or fraud as determined by a court of competent jurisdiction."

We intend to enter into indemnification agreements with each of our directors and officers. These indemnification agreements may require us, among other things, to indemnify our directors and officers for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of our directors or officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request.

We maintain a general liability insurance policy that covers certain liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of ordinary shares being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended, or the Securities Act, against certain liabilities.

### **Item 15. Recent Sales of Unregistered Securities.**

Set forth below is information regarding shares of capital stock issued by us within the past three years. Also included is the consideration received by us for such shares and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of Capital Stock.

From April 24, 2015 through March 2, 2018, the registrant issued an aggregate (i) 4,078,320 Series A Ordinary Shares for aggregate consideration of approximately \$8.7 million, (ii) 21,779,382 Series A Ordinary Shares for nominal consideration to the registrant's founders, (iii) 7,077,298 Series A Ordinary Shares in

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connection with acquisitions for aggregate consideration of approximately \$14.2 million, (iv) 709,210 Series A Ordinary Shares in connection with consulting agreements for aggregate consideration of approximately \$1.4 million, (v) 2,705,550 Series A Ordinary Shares in connection with service agreements for aggregate consideration of approximately \$5.4 million and (vi) 35,000 Series A Ordinary Shares in connection with license agreements for aggregate consideration of approximately \$52,000, to accredited investors, all pursuant to section 4(a)(2) of the Securities Act and Rule 506 as transactions not involving a public offering.

On July 24, 2017, the registrant issued 5,000 Series A Ordinary Shares pursuant to stock options exercised by an employee in connection with services provided to the registrant by the employee pursuant to Section 4(a)(2) and Rule 701 of the Securities Act as transactions not involving a public offering.

From October 1, 2015 through April 12, 2018, the registrant issued an aggregate (i) 39,940,891 Series C Preferred Shares for aggregate consideration of approximately \$107.8 million, including \$1.4 million in converted payables and \$1.2 million of transition services rendered, (ii) 925,926 Series C Preferred Shares in converted promissory notes upon the cancellation of principal debt totaling \$2.5 million principal plus \$145,933 accrued interest, and (iii) 170,370 Series C Preferred Shares in connection with research and license agreements for aggregate consideration approximately \$0.5 million pursuant to Section 4(a)(2) and Rule 506 of the Securities Act.

### (b) Equity Grants.

From March 4, 2016 through January 10, 2018, the registrant granted stock options to purchase an aggregate of 6,292,500 Series A Ordinary Shares with exercise prices ranging between \$0.68 and \$1.99 per share to employees, non-employee consultants, and directors in connection with services provided to the registrant by such parties pursuant to Section 4(a)(2) and Rule 701 of the Securities Act.

### (c) Warrants.

On September 22, 2017, the registrant issued a warrant to purchase up to an aggregate of 2,700,000 shares of Series C preferred shares to Perceptive Life Sciences Master Fund, Ltd pursuant to Section 4(a)(2) and Rule 506 of the Securities Act as a transaction not involving a public offering.

On November 2, 2017, the registrant issued a warrant to purchase up to aggregate of 900,000 shares of Series C preferred shares to Alexandria Equities No. 7, LLC pursuant to Section 4(a)(2) and Rule 506 of the Securities Act as a transaction not involving a public offering.

### (d) Issuance of Notes.

On May 1, 2017, the registrant issued a convertible note to an entity affiliated with Alexandria Equities No. 7, LLC, in the principal amount of \$2.5 million. On November 2, 2017, the convertible note was converted and the registrant issued 925,926 Series C preferred shares to Alexandria Equities No. 7, LLC at \$2.70 per share for an aggregate consideration of approximately \$2.5 million.

On October 26, 2017, the registrant issued a promissory note to Alexandria Equities No. 7, LLC in the principal amount of approximately \$1.4 million.

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### Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

<u>Exhibit Number</u>	<u>Description of Exhibit</u>
1.1*	Underwriting Agreement
3.1*	Articles of Association of the Registrant (currently in effect)
3.2*	Form of Restated Articles of Association of the Registrant (to be effective upon the closing of this offering)
4.1*	Specimen Stock Certificate evidencing the ordinary shares of the Registrant
4.2*	Form of Shareholder Agreement (to be effective upon consummation of the Reorganization Transaction)
5.1*	Opinion of Latham & Watkins LLP
5.2*	Opinion of Walkers
10.1#*	2016 Equity Incentive Plan, as amended, and form of option agreements thereunder
10.2#*	2018 Incentive Award Plan and form of option agreements thereunder
10.3#*	Non-Employee Director Compensation Program
10.4#*	Form of Indemnification Agreement for Directors and Officers
10.5	<a href="#">Lease Agreement, dated June 29, 2016, as amended, between MeiraGTx Limited and ARE-East River Science Park LLC</a>
10.6	<a href="#">Lease Agreement, effective February 2, 2016, among MeiraGTx Limited, Moorfields Eye Hospital NHS, Foundation Trust and Kadmon Corporation LLC</a>
10.7#*	Employment Agreement, dated February 15, 2016, between MeiraGTx Limited and Alexandria Forbes, Ph.D.
10.8#*	Employment Agreement, dated February 15, 2016 between MeiraGTx Limited and Richard Giroux
10.9#*	Employment Agreement, dated April 27, 2015, between MeiraGTx Limited and Stuart Naylor, Ph.D.
10.10*†	License Agreement, dated May 1, 2013, as amended, among MeiraGTx Limited, Brandeis University and BRI-Alzan Inc.
10.11*†	License Agreement, dated February 4, 2015, as amended, between Athena Vision Ltd. and UCL Business, Plc
10.12*†	License Agreement, dated July 28, 2017, as amended, between MeiraGTx UKII Limited and UCL Business, Plc
10.13*†	License Agreement, dated March 15, 2018, among MeiraGTx Limited, MeiraGTx UKII-Limited and UCL Business Plc
10.14*†	Agreement and Plan of Merger, dated December 31, 2015, among MeiraGTx Acquisition Corporation, BRI-Alzan, Inc., F-Prime Inc., Gregory Petsko, Dagmar Ringe, Brandeis University and MeiraGTx Limited
21.1*	Subsidiaries of the Registrant
23.1	<a href="#">Consent of Ernst &amp; Young LLP</a>
23.2*	Consent of Latham & Watkins LLP (included in Exhibit 5.1)
23.3*	Consent of Walkers (included in Exhibit 5.2)
24.1	<a href="#">Power of Attorney (included on signature page)</a>



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- \* To be filed by amendment.  
# Indicates management contract or compensatory plan.  
† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment pursuant to Rule 406 under the Securities Act of 1933, as amended.

### (b) Financial Statement Schedules.

Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the consolidated financial statements or notes thereto.

### **Item 17. Undertakings.**

The undersigned registrant hereby undertakes to provide to the underwriter, at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

## SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of New York, New York, on this 14th day of May, 2018.

MeiraGTx Holdings plc

By: /s/ Alexandria Forbes, Ph.D.  
Alexandria Forbes, Ph.D.  
President and Chief Executive Officer

## SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of MeiraGTx Holdings plc to be appointed prior to the date of the offering, hereby severally constitute and appoint Alexandria Forbes, Ph.D. and Richard Giroux, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities held on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Alexandria Forbes, Ph.D.</u> Alexandria Forbes, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	May 14, 2018
<u>/s/ Richard Giroux</u> Richard Giroux	Chief Operating Officer (principal financial officer and principal accounting officer) and MeiraGTx Holdings plc's authorized representative in the United States	May 14, 2018
<u>/s/ Keith R. Harris, Ph.D.</u> Keith R. Harris, Ph.D.	Chairman of the Board of Directors	May 14, 2018
<u>/s/ Ellen Hukkelhoven, Ph.D.</u> Ellen Hukkelhoven, Ph.D.	Director	May 14, 2018
<u>/s/ Arnold J. Levine, Ph.D.</u> Arnold J. Levine, Ph.D.	Director	May 14, 2018
<u>/s/ Joel S. Marcus</u> Joel S. Marcus	Director	May 14, 2018

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<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Neil Mendoza</u> Neil Mendoza	Director	May 14, 2018
<u>/s/ Gregory S. Moss</u> Gregory S. Moss	Director	May 14, 2018
<u>/s/ Stuart Naylor, Ph.D.</u> Stuart Naylor, Ph.D.	Director	May 14, 2018
<u>/s/ Thomas E. Shenk, Ph.D.</u> Thomas E. Shenk, Ph.D.	Director	May 14, 2018

## LEASE AGREEMENT

THIS LEASE AGREEMENT is made as of this 29 day of June, 2016, between ARE-EAST River Science Park, LLC, a Delaware limited liability company (“**Landlord**”), and MeiraGTx, LLC, a Delaware limited liability company (“**Tenant**”).

## BASIC LEASE PROVISIONS

<b>Address:</b>	430 East 29 <sup>th</sup> Street, New York, New York, 10016.
<b>Premises:</b>	That portion of the Project, containing approximately 5,342 rentable square feet (as determined by Landlord and accepted for all purposes by Tenant), in Suites 1020 and 1030 on the tenth (10 <sup>th</sup> ) floor in the 418,639 rentable square foot West Tower (the “ <b>Building</b> ”) of The Alexandria Center for Life Science - New York City (collectively, together with the underlying land, related site improvements and the immediately adjacent East Tower, the “ <b>Project</b> ”), as shown on <b>Exhibit A</b> .
<b>Shared Lab Area:</b>	That portion of the Building on the tenth floor, as shown on <b>Exhibit N</b> .
<b>Project:</b>	The Alexandria Center for Life Science - New York City, including the Land, all buildings (including the Building) and other improvements located (or to be located) thereon and appurtenances thereto.
<b>Base Rent:</b>	\$491,464.00 per annum, payable in advance in equal monthly installments of \$40,955.33.
<b>Building:</b>	The approximately 418,639 rentable square foot building known as the West Tower of the Project (the “ <b>West Tower</b> ”).
<b>Building’s Share:</b>	The proportionate share of the Project attributed to the Building is 57.53%.
<b>Land:</b>	That certain real property more particularly described on <b>Exhibit B</b> .
<b>Tenant’s Share:</b>	1.276%.
<b>Tenant’s Share (SLA):</b>	17.57%.
<b>Security Deposit:</b>	\$122,866.00.
<b>Target Commencement Date:</b>	On or prior to July 1, 2016.
<b>Rent Commencement Date:</b>	Commencement Date.
<b>Rent Adjustment Percentage:</b>	3.5%
<b>Base Term:</b>	Beginning on the Commencement Date and ending sixty-six (66) months from the first day of the first full calendar month of the Term (as defined in <u>Section 2</u> ) hereof.

**Permitted Use:**

Research and development laboratory, related office and other related uses consistent with the character of the Project and otherwise in compliance with the provisions of Section 7 hereof.

**Address for Rent Payment via Regular Mail:**

P.O. Box 975383  
Dallas, TX 75397-5383

**Address for Rent Payment via Overnight Courier:**

JP Morgan Chase  
Alexandria Real Estate Equities  
Lockbox 975383 TX1-0006  
14800 Frye Road  
Fort Worth, TX 76155

**Wire/ACH Payment Information:**

**Bank Name:** JPMorgan Chase Bank NA  
**Bank Address:** 201 N. Central Ave.  
Phoenix, AZ 85004  
**Account Name:** Alexandria Real Estate  
Equities, Inc.  
**Account Number:**  
**Wire ABA Number:**  
**ACH ABA Number:**

**Tenant's Notice Address:**

Prior to Tenant's occupancy:

MeiraGTx LLC  
450 East 29th Street  
New York, NY 10016

Upon Tenant's occupancy:

MeiraGTx, LLC 430 East 29th Street, Suites 1020 and 1030  
New York, NY 10016

**Landlord's Notice Address:**

385 East Colorado Blvd., Suite 299 Pasadena,  
CA 91101

Attention: Corporate Secretary

The following Exhibits and Addenda are attached hereto and incorporated herein by this reference:

- EXHIBIT A** - PREMISES DESCRIPTION
- EXHIBIT C** - INTENTIONALLY OMITTED
- EXHIBIT E** - RULES AND REGULATIONS
- EXHIBIT G** - INTENTIONALLY OMITTED
- EXHIBIT I** - SHARED LAB SYSTEMS
- EXHIBIT K** - INTENTIONALLY OMITTED
- EXHIBIT M** - SUPERIOR INSTRUMENT EXCERPTS

- EXHIBIT B** - DESCRIPTION OF PROJECT
- EXHIBIT D** — COMMENCEMENT DATE
- EXHIBIT F** - TENANT'S PERSONAL PROPERTY
- EXHIBIT H** - INTENTIONALLY OMITTED
- EXHIBIT J** - ADDITIONAL INSUREDS
- EXHIBIT L** - OPEN SPACE DESCRIPTION
- EXHIBIT N** - SHARED LAB AREA

1. **Lease of Premises.** Upon and subject to all of the terms and conditions hereof, Landlord hereby leases the Premises to Tenant and Tenant hereby leases the Premises from Landlord. Tenant shall have a license, on a non-exclusive basis in common with other tenants and users of the Project, to use all of the Building's public hallways, lobbies, fitness center, corridors and passages and the Building's public stairways as "Common Areas" from time to time, in accordance with the Rules and Regulations applicable thereto and all Legal Requirements; but "Common Areas" shall not include any area within the Premises or any other leased or leasable area of the Project, and such access and use shall be subject to the terms of the Superior Instruments (as defined in Section 27). Landlord reserves the right to modify, from time to time, the Project, the Building, the Open Space and the Common Areas, provided that such modifications do not materially adversely affect Tenant's use of the Premises for the Permitted Use. No vault or cellar is leased hereunder, anything to the contrary indicated elsewhere in this Lease notwithstanding. As used herein, the term "**Open Space**" shall mean the portion of the Project that will be subject to a permanent and perpetual public use and access easement, of a location and size substantially as shown on **Exhibit L**, or otherwise in accordance with the Declaration (Corrective) dated December 29, 2006 by ARE-East River Science Park, LLC, recorded February 20, 2007 at CRFN 2007000094401, as the same may be modified from time to time.

2. **Delivery; Landlord's Work; Acceptance of Premises; Commencement Date.** Landlord shall use reasonable efforts to deliver the Premises to Tenant on or before the Target Commencement Date, with Landlord's Work, if any, Substantially Completed ("**Delivery**" or "**Deliver**"). "**Landlord's Work**" shall mean the completion of the core and shell of the building and completion of the Shared Lab Area and installation of the Shared Lab Systems (as hereinafter defined) in substantial conformance with the Exhibits to this Lease. "**Substantially Completed**" and "**Substantial Completion**" shall mean the completion of Landlord's Work, subject only to punch list items which do not materially impact Tenant's use of the Premises. Tenant shall be solely responsible for ensuring that the Shared Lab Area, the Building and tenant improvement designs and specifications are consistent with Tenant's requirements. Tenant shall solely be responsible for all costs incurred by Landlord to alter the Building as a result of Tenant's requested changes, if any, which changes shall be subject to approval by Landlord in its sole discretion. Landlord shall have no obligation to, and shall not, secure any permits, approvals or entitlements related to Tenant's specific use of the Premises or Tenant's business operations therein. Except as set forth in this Section 2, Landlord shall have no obligation to perform any work at the Project in connection with preparing the Premises for, or accommodating, Tenant's occupancy. If Landlord fails to timely Deliver the Premises, Landlord shall not be liable to Tenant for any loss or damage resulting therefrom, and this Lease shall not be void or voidable, provided that Landlord shall remain obligated to use its commercially reasonable efforts in accordance with the terms hereof to Deliver the Premises. Tenant expressly waives any right to rescind this Lease under Section 223-a of the New York Real Property Law or under any present or future statute of similar import then in force and further expressly waives the right to recover any damages, direct or indirect, which may result from Landlord's failure to deliver possession of the Premises by the Target Commencement Date or to grant access to certain portions of the Premises prior to the Target Commencement Date as permitted hereunder. Tenant agrees that the provisions of this Section 2 are intended to constitute "an express provision to the contrary" within the meaning of said Section 223-a.

(a) The “**Commencement Date**” shall be the earliest of: (i) the date Landlord Delivers the Premises to Tenant; (ii) the date Landlord could have Delivered the Premises but for Tenant Delays; and (iii) the date Tenant conducts any business in the Premises or any part thereof. Upon request of Landlord, Tenant shall execute and deliver a written acknowledgment of the Commencement Date and the expiration date of the Term when such are established in the form of the “Acknowledgement of Commencement Date” attached to this Lease as **Exhibit D**; provided, however, Tenant’s failure to execute and deliver such acknowledgment shall not affect Landlord’s rights hereunder. The “**Term**” of this Lease shall be the Base Term, as defined above in the Basic Lease Provisions.

(b) Tenant shall accept the Premises in their “AS-IS” condition as of the Commencement Date, and, other than Landlord’s Work, Landlord shall have no obligation for any defects in the Premises, to perform any work or make any installations in order to prepare the Premises for Tenant’s occupancy. Tenant’s taking possession of the Premises shall be conclusive evidence that Tenant accepts the Premises and that the Premises were in good condition at the time possession was taken. Any occupancy of the Premises by Tenant before the Commencement Date shall be subject to all of the terms and conditions of this Lease, including the obligation to pay Rent.

(c) Tenant agrees and acknowledges that neither Landlord nor any agent of Landlord has made any representation or warranty with respect to the condition of all or any portion of the Premises, the Building or the Project, and/or the suitability of the Premises, the Building or the Project for the conduct of Tenant’s business, and Tenant waives any implied warranty that the Premises, the Building or the Project are suitable for the Permitted Use. No rights, easements or licenses are acquired by Tenant by implication or otherwise except as expressly set forth in this Lease. This Lease constitutes the complete agreement of Landlord and Tenant with respect to the subject matter hereof and supersedes any and all prior representations, inducements, promises, agreements, understandings and negotiations which are not contained herein. Landlord in executing this Lease does so in reliance upon Tenant’s representations, warranties, acknowledgments and agreements contained herein.

### 3. **Rent.**

(a) **Base Rent.** The first month’s Base Rent and the Security Deposit shall be due and payable on delivery of an executed copy of this Lease to Landlord. Tenant shall pay to Landlord in advance, without demand, abatement, deduction or set-off, monthly installments of Base Rent on or before the first day of each calendar month during the Term hereof, in lawful money of the United States of America, at the office of Landlord for payment of Rent set forth above, or to such other person or at such other place as Landlord may from time to time designate in writing. Payments of Base Rent for any fractional calendar month shall be prorated. The obligation of Tenant to pay Base Rent and other sums to Landlord and the obligations of Landlord under this Lease are independent obligations. Tenant shall have no right at any time to abate, reduce, or set-off any Rent (as defined in Section 5) due hereunder except for any abatement as may be expressly provided in this Lease.

(b) **Additional Rent.** In addition to Base Rent, Tenant agrees to pay to Landlord as additional rent (“**Additional Rent**”): (i) Tenant’s Share of “Operating Expenses” (as defined in

Section 5, (ii) administrative rent for property management services in the amount of 3.00% of the Base Rent (determined without regard to any rent abatement that may be applicable) (“**Administrative Rent**”) and (iii) any and all other amounts Tenant assumes or agrees to pay under the provisions of this Lease, including, without limitation, any and all other sums that may become due by reason of any default of Tenant or failure to comply with the agreements, terms, covenants and conditions of this Lease to be performed by Tenant, after any applicable notice and cure period.

4. **Base Rent Adjustments.** Base Rent shall be increased on each annual anniversary of the first day of the first full month during the Term of this Lease (each an “**Adjustment Date**”) by multiplying the Base Rent payable immediately before such Adjustment Date by the Rent Adjustment Percentage and adding the resulting amount to the Base Rent payable immediately before such Adjustment Date. Base Rent, as so adjusted, shall thereafter be due as provided herein. Base Rent adjustments for any fractional calendar month shall be prorated. Notwithstanding anything to the contrary contained in this Lease, but provided Tenant is not in Default hereunder, Landlord hereby grants Tenant an abatement of the Base Rent payable during the period beginning on the Commencement Date and ending six (6) months after the Commencement Date (“**Base Rent Abatement**”). For the avoidance of doubt, if the Commencement Date occurs on the first day of a month, the Base Rent Abatement will be measured from that date. If the Commencement Date occurs on a day other than the first day of a month, the Base Rent Abatement will be measured from the first day of the following month. Except as provided in the preceding sentences, Tenant shall pay the full amount of Base Rent due in accordance with the provisions of this Lease. The Administrative Rent set forth in Section 3(b) above and the Operating Expenses set forth in Section 5 below shall not be abated and shall be based on the amount of Base Rent that would have been payable but for the Base Rent Abatement. Notwithstanding anything to the contrary in this Section 4, the adjustment in the Base Rent as set forth in this Section 4 shall be based on the full and unabated amount of Base Rent payable for the first 12 month period from and after the Commencement Date.

5. **Operating Expense Payments.** Landlord shall deliver to Tenant a written estimate of Operating Expenses for each calendar year during the Term (the “**Annual Estimate**”), which may be revised by Landlord from time to time during such calendar year. During each month of the Term, on the same date that Base Rent is due, Tenant shall pay Landlord an amount equal to 1/12<sup>th</sup> of Tenant’s Share of the Annual Estimate. Payments for any fractional calendar month shall be prorated.

(a) The term “**Operating Expenses**” means all costs and expenses of any kind or description whatsoever incurred or accrued each calendar year by Landlord with respect to the Building (including the Building’s Share of all costs and expenses of any kind or description incurred or accrued by Landlord with respect to the Project which are not specific to the Building or any other building located in the Project) (including, without duplication, Taxes (as defined in Section 9), all Building and project related costs in connection with the shell and core of the Building, site improvements, transportation, maintenance, common area utilities, taxes, real estate taxes or PILOT payments, insurance and capital repairs and improvements amortized (with interest at the Default Rate) over the lesser of 7 years and the useful life of such capital items), and the costs and expenses of maintaining, repairing, replacing and operating the Shared Lab Area and the Shared Lab Systems (as such terms are defined in Section 46). excluding only:

- (i) the original construction costs of the Project and costs of correcting defects in such original construction;



(ii) capital expenditures for expansion of the Project;

(iii) interest, principal payments of any Mortgage (as defined in Section 27) debts of Landlord, financing costs and amortization of funds borrowed by Landlord, whether secured or unsecured and all payments of base rent (but not taxes or operating expenses) under any ground lease or other underlying lease of all or any portion of the Project;

(iv) depreciation of the Project (provided that the exclusion of depreciation shall not preclude inclusion of amortization of capital improvements, which is includable in Operating Expenses in accordance with the terms of this Lease);

(v) advertising, legal and space planning expenses and leasing commissions and other costs and expenses incurred in procuring and leasing space to tenants for the Project, including any leasing office maintained in the Project, free rent and construction allowances for tenants;

(vi) legal and other expenses incurred in the negotiation or enforcement of leases;

(vii) costs of completing, fixturing, improving, renovating, painting, redecorating or other work, which Landlord pays for or performs for other tenants within their premises, and costs of correcting defects in such work; in each instance other than those ordinary building repairs and maintenance to Building structures, windows and Building Systems;

(viii) costs to be reimbursed by other tenants of the Project or Taxes to be paid directly by Tenant or other tenants of the Project, whether or not actually paid;

(ix) salaries, wages, benefits and other compensation paid to officers and employees of Landlord who are not assigned in whole or in part to the operation, management, maintenance or repair of the Project;

(x) general organizational, administrative and overhead costs relating to maintaining Landlord's existence, either as a corporation, partnership, or other entity, including general corporate, legal and accounting expenses;

(xi) costs (including attorneys' fees and costs of settlement, judgments and payments in lieu thereof) incurred in connection with disputes with tenants, other occupants, or prospective tenants, and costs and expenses, including legal fees, incurred in connection with negotiations or disputes with employees, consultants, management agents, leasing agents, purchasers or mortgagees of the Building;

(xii) costs incurred by Landlord due to the violation by Landlord, its employees, agents or contractors or any tenant of the terms and conditions of any lease of space in the Project or any Legal Requirement (as defined in Section 7);

(xiii) penalties, fines or interest incurred as a result of Landlord's inability or failure to make payment of Taxes and/or to file any tax or informational returns when due, or from Landlord's failure to make any payment of Taxes required to be made by Landlord hereunder before delinquency;

(xiv) overhead and profit increment paid to Landlord or to subsidiaries or affiliates of Landlord for goods and/or services in or to the Project to the extent the same materially exceeds the costs of such goods and/or services rendered by unaffiliated third parties on a competitive basis;

(xv) costs of Landlord's charitable or political contributions, or of fine art maintained at the Project;

(xvi) costs in connection with services (including electricity), items or other benefits of a type which are not standard for the Project and which are not available to Tenant without specific charges therefor, but which are provided to another tenant or occupant of the Project, whether or not such other tenant or occupant is specifically charged therefor by Landlord;

(xvii) costs incurred in the sale or refinancing of the Project;

(xviii) subject to Section 9(a), net income taxes of Landlord or the owner of any interest in the Project, franchise, capital stock, gift, estate or inheritance taxes or any federal, state or local documentary taxes imposed against the Project or any portion thereof or interest therein; and

(xix) any expenses otherwise includable within Operating Expenses to the extent actually reimbursed by persons other than tenants of the Project under leases for space in the Project.

(b) Within 120 days after the end of each calendar year (or such longer period as may be reasonably required), Landlord shall furnish to Tenant a statement (an "**Annual Statement**") showing in reasonable detail: (a) the total and Tenant's Share of actual Operating Expenses for the previous calendar year, and (b) the total of Tenant's payments in respect of Tenant's Share of Operating Expenses for such year. If Tenant's Share of actual Operating Expenses for such year exceeds Tenant's payments of Tenant's Share of Operating Expenses for such year, then the excess shall be due and payable by Tenant as Rent within 30 days after delivery of such Annual Statement to Tenant. If Tenant's payments of Operating Expenses for such year exceed Tenant's Share of actual Operating Expenses for such year, then Landlord shall pay the excess to Tenant within 30 days after delivery of such Annual Statement, except that after the expiration, or earlier termination of the Term or if Tenant is delinquent in its obligation to pay Rent, Landlord shall pay the excess to Tenant after deducting all other amounts due Landlord.

(c) Each Annual Statement shall be final and binding upon Tenant unless Tenant, within 30 days after Tenant's receipt thereof, shall contest any item therein by giving written notice to Landlord, specifying each item contested and the reason therefor. Operating Expenses for the calendar years in which Tenant's obligation to share therein begins and ends shall be prorated. Notwithstanding anything set forth herein to the contrary, if the Building is not at least 95% occupied on average during any year of the Term, Tenant's Share of Operating Expenses for such

year shall be computed as though the Building had been 95% occupied on average during such year. “**Tenant’s Share**” shall be the percentage set forth in the Basic Lease Provisions as Tenant’s Share as reasonably adjusted by Landlord. Landlord may equitably increase Tenant’s Share (or Tenant’s Share of Operating Expenses, as the case may be) for any item of expense or cost reimbursable by Tenant that relates to a repair, replacement, or service that benefits only the Premises or only a portion of the Project that includes the Premises or that varies with occupancy or use. Base Rent, Additional Rent (including Tenant’s Share of Operating Expenses) and other amounts payable by Tenant to Landlord hereunder are collectively referred to herein as “**Rent**.”

## 6. Security Deposit.

(a) Tenant shall deposit with Landlord, upon delivery of an executed copy of this Lease to Landlord, a security deposit (the “**Security Deposit**”) for the performance of all of Tenant’s obligations hereunder in the amount set forth in the Basic Lease Provisions, which Security Deposit shall be in the form of an unconditional and irrevocable letter of credit (the “**Letter of Credit**”): (i) in form and substance satisfactory to Landlord, (ii) naming Landlord as beneficiary, (iii) expressly allowing Landlord to draw upon it at any time from time to time by delivering to the issuer notice that Landlord is entitled to draw thereunder, (iv) issued by an FDIC-insured financial institution satisfactory to Landlord, and (v) redeemable by presentation of a sight draft in the state of Landlord’s choice. If Tenant does not provide Landlord with a substitute Letter of Credit complying with all of the requirements hereof at least 30 days before the stated expiration date of any then current Letter of Credit, Landlord shall have the right to draw the full amount of the current Letter of Credit and hold the funds drawn in cash without obligation for interest thereon as the Security Deposit. The Security Deposit shall be held by Landlord as security for the performance of Tenant’s obligations under this Lease. The Security Deposit is not an advance rental deposit or a measure of Landlord’s damages in case of Tenant’s default. Upon each occurrence of a Default (as defined in Section 20). Landlord may use all or any part of the Security Deposit to pay delinquent payments due under this Lease, and the cost of any damage, injury, expense or liability caused by such Default, without prejudice to any other remedy provided herein or provided by law. Upon any such use of all or any portion of the Security Deposit, Tenant shall pay Landlord on demand the amount that will restore the Security Deposit to the amount set forth in the Basic Lease Provisions or Tenant shall promptly provide Landlord with an amendment to the Letter of Credit reflecting and ratifying Landlord’s draw thereunder and Tenant’s subsequent restoration of the Letter of Credit to the original amount. Tenant hereby waives the provisions of any law, now or hereafter in force, which provide that Landlord may claim from a security deposit only those sums reasonably necessary to remedy defaults in the payment of Rent, to repair damage caused by Tenant or to clean the Premises, it being agreed that Landlord may, in addition, claim those sums reasonably necessary to compensate Landlord for any other loss or damage, foreseeable or unforeseeable, caused by the act or omission of Tenant or any officer, employee, agent or invitee of Tenant. Upon bankruptcy or other debtor-creditor proceedings against Tenant, the Security Deposit shall be deemed to be applied first to the payment of Rent and other charges due Landlord for periods prior to the filing of such proceedings. Upon any such use of all or any portion of the Security Deposit, Tenant shall, within 5 days after demand from Landlord, restore the Security Deposit to its original amount. If Tenant shall fully perform every provision of this Lease to be performed by Tenant, the Security Deposit, or any balance thereof (i.e., after deducting therefrom all amounts to which Landlord is entitled under the provisions of this Lease), shall be returned to Tenant (or, at Landlord’s option, to the last assignee of Tenant’s interest hereunder) within 90 days

after the expiration or earlier termination of this Lease. In the event the issuer of the Letter of Credit experiences a downgrade of its debt rating below "A-" by Standard & Poors Rating Services, a division of The McGraw-Hill Companies, Inc. ("**S&P**") or the equivalent rating by Moody's Investor Services, Inc. ("**Moody's**") at any time during which Tenant is obligated to provide the Letter of Credit, Landlord shall be entitled, in Landlord's sole discretion, to receive a replacement Letter of Credit from an issuing bank with a debt rating of "AA" by S&P or the equivalent rating by Moody's (or better).

(b) If Landlord transfers its interest in the Project or this Lease, Landlord shall either (a) transfer any Security Deposit then held by Landlord to a person or entity assuming Landlord's obligations under this Section 6, or (b) return to Tenant any Security Deposit then held by Landlord and remaining after the deductions permitted herein. Upon such transfer to such transferee or the return of the Security Deposit to Tenant, Landlord shall have no further obligation with respect to the Security Deposit, and Tenant's right to the return of the Security Deposit shall apply solely against Landlord's transferee. The Security Deposit is not an advance rental deposit or a measure of Landlord's damages in case of Tenant's default. Landlord's obligation respecting the Security Deposit is that of a debtor, not a trustee, and no interest shall accrue thereon.

(c) Tenant covenants that it will not assign or encumber, or attempt to assign or encumber, the Security Deposit. Neither Landlord, nor its successors or assigns, shall be bound by any such assignment, encumbrance, attempted assignment or attempted encumbrance. It is agreed that the provisions of this Section shall apply to every sale, transfer or assignment made of the security to a new Landlord. Tenant shall pay and be liable for any and all fees arising from any transfer of the Letter of Credit upon transfers of ownership of the Project, Building or Premises.

## 7. Use.

(a) Tenant shall have 24 hours per day, 7 days per week access to its Premises, the Building and the parking area, subject to restricted access due to Force Majeure, necessary for repairs or emergency conditions, or arising due to Legal Requirements. Tenant shall use the Premises solely for the Permitted Use set forth in the Basic Lease Provisions, and in compliance with all present and future laws, orders, judgments, ordinances, regulations, codes, directives, permits, licenses, covenants and restrictions of all state, federal, municipal and local governments, departments, commissions and boards and any direction of any public officer pursuant to law, and all orders, rules and regulations of the New York Board of Fire Underwriters, Insurance Services Office, or any similar body, in each case, applicable to the Premises and the use and occupancy thereof, including, without limitation, the Americans With Disabilities Act, 42 U.S.C. § 12101, et seq. (together with the regulations promulgated pursuant thereto, "**ADA**") (collectively, "**Legal Requirements**" and each, a "**Legal Requirement**"). Tenant shall not occupy, use or operate the Premises, or allow the Premises or any part thereof to be occupied, used or operated for any unlawful purpose or in violation of any certificate of occupancy affecting the Building and/or the Project or for any use that may constitute a nuisance, public or private. Tenant shall not permit any part of the Premises to be used as a "place of public accommodation", as defined in the ADA or any similar legal requirement. Tenant will use the Premises in a careful, safe and proper manner and will not commit or permit waste, overload the floor or structure of the Premises, subject the Premises to any use that would damage the Premises or obstruct or interfere with the rights of Landlord or other tenants or occupants of the Project, including, without limitation, conducting or giving notice of any auction, liquidation, or going out of business sale on the Premises.

(b) Immediately upon its discovery of any violation or breach of any Legal Requirement, this Lease or any Superior Instrument, Tenant shall take all necessary steps, legal and equitable, to compel the cure of such violation or breach, including, if necessary, the removal from the Premises of any subtenants or licensees using a portion of the Premises.

(c) Tenant will not use or permit the Premises to be used for any purpose or in any manner that is prohibited under the Ground Lease (as defined in Section 27) or that would void Tenant's, Landlord's or the Condominium Board's insurance, increase the insurance risk, or cause the disallowance of any sprinkler or other credits.

(d) Tenant shall reimburse Landlord or the Condominium Board, as applicable, promptly upon demand for any additional premium charged for any such insurance policy by reason of Tenant's failure to comply with the provisions of this Section 7 or otherwise caused by Tenant's use and/or occupancy of the Premises.

(e) Tenant shall cause any equipment or machinery to be installed in the Premises so as to reasonably prevent odors, sounds or vibrations from the Premises from extending into Common Areas, or other space in the Project. Tenant shall not place any machinery or equipment weighing 500 pounds or more in or upon the Premises or transport or move such items through the Common Areas of the Project or in the Project elevators without the prior written consent of Landlord. Landlord reserves the right to prescribe the weight and position of all safes, files, paper and book storage facilities, business machines and other heavy equipment and installations.

(f) Tenant shall not, without the prior written consent of Landlord, use the Premises in any manner which will require ventilation, air exchange, heating, gas, steam, electricity or water beyond the existing capacity of the Project as proportionately allocated to the Premises based upon Tenant's Share as usually furnished for the Permitted Use, nor shall Tenant use the Premises in a manner that results in transmissions from the Premises at a frequency which interferes with any other tenant's use of any portion of the Building or the Project other than the Premises.

(g) Tenant shall not use the Premises or any part thereof, or permit the Premises or any part thereof to be used for the preparation, dispensing, consumption or sale of food or beverages in any manner whatsoever, whether for "on" or "off" premises consumption (other than the consumption of food by employees and invitees of Tenant).

Landlord shall, as an Operating Expense (to the extent such Legal Requirement is generally applicable to similar buildings in the area in which the Project is located) or at Tenant's expense (to the extent such Legal Requirement is applicable solely by reason of Tenant's, as compared to other tenants of the Project, particular use of the Premises) make any alterations or modifications to the Common Areas or the exterior of the Building that are required by Legal Requirements, including the ADA. Tenant, at its sole expense, shall make any alterations or modifications to the interior of the Premises that are required by Legal Requirements (including, without limitation, compliance of the Premises with the ADA). Notwithstanding any other provision herein to the contrary, Tenant shall be responsible for any and all demands, claims, liabilities, losses, costs,

expenses, actions, causes of action, damages or judgments, and all reasonable expenses incurred in investigating or resisting the same (including, without limitation, reasonable attorneys' fees, charges and disbursements and costs of suit) (collectively, "Claims") arising out of or in connection with Legal Requirements, and Tenant shall indemnify, defend, hold and save Landlord harmless from and against any and all Claims arising out of or in connection with any failure of the Premises to comply with any Legal Requirement.

**8. Holding Over.** If, with Landlord's express written consent, Tenant retains possession of the Premises after the expiration or earlier termination of the Term, (i) unless otherwise agreed in such written consent, such possession shall be subject to immediate termination by Landlord at any time, or shall become a tenant at sufferance upon the terms described herein below, (ii) all of the other terms and provisions of this Lease (including, without limitation, the adjustment of Base Rent pursuant to Section 4 hereof) shall remain in full force and effect (excluding any expansion or renewal option or other similar right or option) during such holdover period, (iii) Tenant shall continue to pay Base Rent in the amount payable upon the date of the expiration or earlier termination of this Lease or such other amount as Landlord may indicate, in Landlord's sole and absolute discretion, in such written consent, and (iv) all other payments shall continue under the terms of this Lease. The parties recognize and agree that the damage to Landlord resulting from any failure by Tenant to timely surrender possession of the Premises as aforesaid will be extremely substantial, will exceed the amount of the monthly installments of the Base Rent and Rental theretofore payable hereunder, and will be impossible to accurately measure. Tenant therefore agrees that if Tenant remains in possession of the Premises after the expiration or earlier termination of the Term without the express written consent of Landlord, then, in addition to any other rights or remedies Landlord may have hereunder or at law, and without in any manner limiting Landlord's right to demonstrate and collect any damages suffered by Landlord and arising from Tenant's failure to surrender the Premises as provided herein, (A) Tenant shall become a tenant at sufferance upon the terms of this Lease except that the monthly rental shall be equal to 200% of the greater of the Rent in effect during the last 30 days of the Term and the then fair market rental value for the Premises, and (B) Tenant shall be responsible for all damages suffered by Landlord resulting from or occasioned by Tenant's holding over, including consequential damages. No holding over by Tenant, whether with or without consent of Landlord, shall operate to extend this Lease except as otherwise expressly provided, and this Section 8 shall not be construed as consent for Tenant to retain possession of the Premises. Acceptance by Landlord of Rent after the expiration of the Term or earlier termination of this Lease shall not result in a renewal or reinstatement of this Lease. The acceptance by Landlord of any such use and occupancy payment by Tenant pursuant to this Section 8 shall in no event preclude Landlord from commencing and prosecuting a holdover or summary eviction proceeding, and the provisions of this Section 8 shall be deemed to be an "agreement expressly providing otherwise" within the meaning of Section 232-c of the Real Property Law of the State of New York and any successor or similar law of like import. Nothing contained in this Section 8 shall (i) imply any right of Tenant to remain in the Premises after the expiration of the Term without the execution of a new lease, (ii) imply any obligation of Landlord to grant a new lease or (iii) be construed to limit any right or remedy that Landlord has against Tenant as a holdover tenant or trespasser and no acceptance by Landlord of payments from Tenant after the Expiration Date shall be deemed to be other than on account of the amount to be paid by Tenant in accordance with the provisions of this Section 8. The provisions of this Section 8 shall survive the expiration or earlier termination of this Lease.

## 9. Taxes.

(a) Landlord shall pay, as part of Operating Expenses, all taxes, levies, fees, assessments and governmental charges of any kind, existing as of the Commencement Date or thereafter enacted (collectively referred to as "**Taxes**"), imposed by any federal, state, regional, municipal, local or other governmental authority or agency, including, without limitation, quasi-public agencies (collectively, "**Governmental Authority**") during the Term, including, without limitation, all Taxes: (i) imposed on or measured by or based, in whole or in part, on rent payable to (or gross receipts received by) Landlord under this Lease and/or from the rental by Landlord of the Project or any portion thereof, or (ii) based on the square footage, assessed value or other measure or evaluation of any kind of the Premises or the Project, or (iii) assessed or imposed by or on the operation or maintenance of any portion of the Premises or the Project, including parking, or (iv) assessed or imposed by, or at the direction of, or resulting from Legal Requirements, or interpretations thereof, promulgated by any Governmental Authority, or (v) imposed as a license or other fee, charge, tax, or assessment on Landlord's business or occupation of leasing space in the Project, or (vi) any taxes or assessments levied after the date of this Lease in whole or in part for public benefits to the Project, including without limitation any Business Improvement District ("**BID**") tax increment financing ("**TIF**") or Commercial Rent Occupancy Tax ("**CROT**") taxes and assessments payable by Landlord and any and all other governmental and quasi-governmental assessments) without taking into account any discount that Landlord may receive by virtue of any early payment of Taxes. Landlord may contest by appropriate legal proceedings the amount, validity, or application of any Taxes or liens securing Taxes. Taxes shall include all payments in lieu of taxes ("**PILOT**") and other impositions and costs for which Landlord is responsible under any Superior Lease (as defined in Section 27) including without limitation under Articles 3 and 4 of the Ground Lease or under the IDA Lease Documents (as defined in Section 27). Taxes shall not take into account any exemption which Landlord is entitled to under any governmental incentive program for investment and/or employment creation where Landlord is the induced party including without limitation the Industrial and Commercial Incentive Program ("**ICIP**") or under the IDA Lease Documents or Ground Lease or any other governmental incentive program. Taxes shall not include any net income taxes, franchise, capital stock, gift, estate or inheritance taxes imposed on Landlord or the owner of any interest in the Project or any federal, state or local documentary taxes imposed against the Project or any portion thereof or interest therein, except to the extent the same, however denominated, are imposed in substitution for any Taxes payable hereunder as a result of any change in the manner of taxation of the ownership or operation of real estate in which case the same shall be deemed to be included within the definition of the term "Taxes." If any such Tax is levied or assessed directly against Tenant, then Tenant shall be responsible for and shall pay the same at such times and in such manner as the taxing authority shall require. Tenant shall pay, prior to delinquency, any and all Taxes levied or assessed against any personal property or trade fixtures placed by Tenant in the Premises, whether levied or assessed against Landlord or Tenant. If any Taxes on Tenant's personal property or trade fixtures are levied against Landlord or Landlord's property, or if the assessed valuation of the Project is increased by a value attributable to improvements in or alterations to the Premises, whether owned by Landlord or Tenant and whether or not affixed to the real property so as to become a part thereof, higher than the base valuation on which Landlord from time-to-time allocates Taxes to all tenants in the Project, Landlord shall have the right, but not the obligation, to pay such Taxes. Landlord's determination of any excess assessed valuation shall be binding and conclusive, absent manifest error. The amount of any such payment by Landlord shall constitute

Additional Rent due from Tenant to Landlord immediately upon demand. With respect to any tax year, all reasonable and customary expenses, including attorneys' fees and disbursements, experts' and other witnesses' fees, incurred in contesting the validity or amount of any Taxes or in obtaining a refund of Taxes shall be considered as part of the Taxes for such tax year. Special assessments, if any, shall be deemed paid in the maximum number of installments allowed by the Governmental Authority having jurisdiction thereover, notwithstanding that Landlord may elect to pay the same on a different schedule. If at any time the methods of taxation prevailing as of the date hereof shall be altered so that in lieu of or as an express substitute for the whole or any part of the Taxes, assessments, rents, rates, charges, levies or impositions now assessed, levied or imposed upon all or any part of the Project or any part thereof, there shall be assessed, levied or imposed (1) a tax, assessment, levy, imposition or charge based on the income or rents received therefrom, whether or not wholly or partially as a capital levy or otherwise, or (2) a tax, assessment, levy, imposition or charge measured by or based in whole or in part upon all or any part of the Project, or (3) a license fee measured by the rents, or (4) any other tax, assessment, levy, imposition, charge or license fee with respect to the Project, or any part thereof, however described or imposed, then all such taxes, assessments, levies, impositions, charges or license fees or the part thereof so measured or based shall be deemed to be Taxes.

(b) Tenant hereby covenants and agrees to (i) pay any and all CROT taxes and assessments payable by Landlord with respect to any rent due hereunder, (ii) pay any and all New York City and New York state transfer taxes, sales taxes and any and all other taxes payable by or on behalf of Tenant, as the same shall become due or payable, and (iii) file all tax returns required to be filed in connection with the foregoing.

10. **Parking.** Subject to all matters of record, Force Majeure, a Taking (as defined in Section 19 below), the terms and conditions of this Lease and the exercise by Landlord of its rights hereunder, Tenant shall have the right, in common with other tenants of the Project pro rata in accordance with the rentable area of the Premises and the rentable areas of the Project occupied by such other tenants, and subject to the payment by Tenant of Landlord's customary parking fees and charges, the payment of which constitutes Rent hereunder, to park in those areas designated for non-reserved parking, subject in each case to Landlord's rules and regulations and subject to the rights of ingress and egress of other tenants and their employees, agents and invitees to other areas of the Project, provided, however, that Landlord shall have the right, without notice in an emergency and otherwise for any reason upon not less than five (5) days' written notice, to relocate all or part of the non-reserved or reserved parking to other locations in the parking areas of the Project, and/or to suspend or terminate the right to use any or all the parking spaces. Landlord may allocate parking spaces among Tenant and other tenants in the Project pro rata as described above if Landlord determines that such parking facilities are becoming crowded. Landlord shall not be responsible for enforcing Tenant's parking rights against any third parties, including other tenants of the Project. If applicable, Tenant shall comply with the Project's transportation plans to be created by Landlord under the guidelines set forth by the City of New York.

11. **Utilities; Services; Refuse and Trash.**

(a) **General.** Landlord shall provide, subject to the terms of this Section 11, water, electricity, heat, steam, air conditioning, ventilating, light, power, telephone, sewer, and fire sprinklers to the extent the Project is plumbed for such services (collectively, "**Utilities**"). Landlord



shall pay for (and shall not include in Operating Expenses) all Utilities used on the Premises, all maintenance charges for Utilities, and any storm sewer charges or other similar charges for Utilities imposed by any Governmental Authority or Utility provider, and any taxes, penalties, surcharges or similar charges thereon. Tenant acknowledges that Landlord is not the generator of Utilities and that Landlord's obligation to deliver Utilities to the Premises pursuant to this Lease consequently is subject to the provision of electrical energy and water service to the Project, as applicable, by the respective utility company responsible for delivering same to the Project. Landlord shall have no liability for the availability, capacity, quality, continuity or character of service of Utilities, and no eviction or constructive eviction of Tenant, termination of this Lease or abatement of Rent shall arise due to, nor shall Landlord have any liability due to any loss, cost, claim, damage or expense arising from the availability, capacity, quality, continuity or character of service of Utilities or any interruption, deterioration or removal of any of the foregoing, except as caused by Landlord's willful misconduct. Tenant acknowledges that the capacity of such utilities available to the Premises is part of the overall capacity of such utilities available to the Project for its use on a nonexclusive basis in common with all other tenants at the Project. Tenant agrees to limit use of water and sewer with respect to Common Areas to normal restroom use.

**(b) Special Provisions Regarding Electricity.**

(i) In the event that any tax shall be imposed upon Landlord's receipts from the sale, use or resale of electrical energy or any other utility service to Tenant, the pro rata share allocable to such service received by Tenant shall be passed onto, included in the bill of, and paid by Tenant if and to the extent not prohibited by applicable Legal Requirements.

(ii) Tenant shall enter into such modifications of this Lease as Landlord may from time to time reasonably request in connection with any requirement of the New York State Public Service Commission, or any successor thereto, or any requirement of law pertaining to the supplying of electrical service or the charges therefor under any provision of the Lease. If because of any such requirement, any provision of this Section cannot be given full effect, whether with respect to any past period or any future period, the parties shall enter into such modifications of the Lease setting forth substitute provisions, consistent with such requirements, which, to the maximum extent possible, achieve the intended purposes of the provisions of this Section which cannot be given full effect.

**(c) Refuse and Trash.** Landlord shall provide refuse and trash collection and janitorial services at the Building for ordinary office refuse and rubbish and cleaning, and the cost of such services shall be included in Operating Expenses. To the extent that the refuse and trash and/or cleaning needs generated by Tenant exceeds the refuse and trash and/or cleaning needs customarily generated by other tenants of the Building, Tenant shall pay to Landlord the costs that Landlord reasonably incurs for such removal and/or cleaning, within 10 days after rendition of bills therefor, as Additional Rent. In respect of refuse and trash other than ordinary office refuse and rubbish (such as bio/medical waste, "wet trash" and construction debris, and cleaning with respect thereto), at Landlord's option (i) Landlord shall provide collection and janitorial services for such refuse and trash, and Tenant shall pay to Landlord an amount equal to 105% of the Landlord's cost therefor, within 10 days after rendition of bills therefor, as Additional Rent, or (ii) Tenant shall contract directly with the third-party service provider (acceptable to Landlord in its sole discretion) for the provision of such services and, in such case, Tenant shall pay such service provider directly,

prior to delinquency. In all cases, Tenant shall store and stage all its waste, refuse, trash and recyclables within its Premises or in such enclosure areas as may be designated by Landlord and shall keep the Premises in a neat and clean condition. Tenant shall not dispose of any refuse in the Common Areas, and if Tenant does so, Tenant shall be liable for Landlord's reasonable charge for such removal. Tenant shall comply with all Legal Requirements, whether imposed on Landlord or Tenant, regarding the collection, sorting, separation and recycling of waste products, garbage, refuse and trash in the Premises and cleaning the Premises. Upon request by Landlord, Tenant shall sort and separate into categories designated by Landlord and shall place in separate receptacles (as may be designated by Landlord) all waste products, garbage, refuse and trash in the Premises.

(d) **Loading Dock and Freight Elevator.** Landlord shall provide, on a non-exclusive, first-come, first-served basis, freight elevator service to the floor on which the Premises are located and access to a loading dock adjacent to such freight elevator for Tenant's deliveries in and out of the Premises in connection with the Permitted Use. Tenant's use of the freight elevator and the loading dock shall be subject to the Superior Instruments, the Rules and Regulations, Landlord's security requirements for the Building and/or the Project, and the terms of this Lease. Landlord shall have the right to change the operation or manner of operation of any of the elevators in the Building and/or to discontinue temporarily the use of any one or more cars in any of the elevator banks provided that at all times there will be at least one passenger elevator serving the Premises at all times (subject to such passenger elevator not being in service due to repairs or alterations being made thereto).

## 12. **Alterations and Tenant's Property.**

(a) Any alterations, additions, or improvements made to the Premises by or on behalf of Tenant, including additional locks or bolts of any kind or nature upon any doors or windows in the Premises, but excluding installation, removal or realignment of furniture systems (other than removal of furniture systems owned or paid for by Landlord) not involving any modifications to the structure of the Building or connections (other than by ordinary plugs or jacks) to Building Systems (as defined in Section 13) ("**Alterations**") shall be subject to Landlord's prior written consent, which may be given or withheld in Landlord's sole discretion if any such Alteration affects the structure of the Building or Building Systems, or if Landlord deems that such proposed Alteration will adversely affect Landlord's ability to re-lease the Premises, but which shall otherwise not be unreasonably withheld or delayed. If Landlord approves any Alterations, Landlord may impose such conditions on Tenant in connection with the commencement, performance and completion of such Alterations as Landlord may deem appropriate in Landlord's reasonable discretion. Any request for approval shall be in writing, delivered not less than 15 business days in advance of any proposed construction, and accompanied by plans, specifications, bid proposals, work contracts and such other information concerning the nature and cost of the Alterations as may be reasonably requested by Landlord, including the identities and mailing addresses of all persons performing work or supplying materials. Landlord's right to review plans and specifications and to monitor construction shall be solely for its own benefit, and Landlord shall have no duty to ensure that such plans and specifications or construction comply with applicable Legal Requirements. Tenant shall cause, at its sole cost and expense, all Alterations to comply with any applicable insurance requirements and with Legal Requirements and shall implement at its sole cost and expense any alteration or modification required by Legal

Requirements as a result of any Alterations. Tenant shall pay to Landlord, as Additional Rent, on demand an amount equal to 3% of all charges incurred by Tenant or its contractors or agents in connection with any Alteration to cover Landlord's overhead and expenses for plan review, coordination, scheduling and supervision. Before Tenant begins any Alteration, Tenant shall post on and about the Premises notices of non-responsibility pursuant to applicable law. Tenant shall reimburse Landlord and the Condominium Board for, and indemnify and hold Landlord and the Condominium Board harmless from, any expense incurred by Landlord and/or the Condominium Board, as applicable, by reason of faulty work done by Tenant or its contractors, delays caused by such work, or inadequate cleanup.

(b) In the event Tenant installs a security system or additional locks, Tenant shall supply Landlord with the necessary card(s) or key(s) and security codes to permit entry in the event of an emergency endangering life or property.

(c) Tenant shall furnish security or make other arrangements satisfactory to Landlord to assure payment for the completion of all Alterations work free and clear of liens, and shall provide (and cause each contractor or subcontractor to provide) certificates of insurance for workers' compensation and other coverage in amounts and from an insurance company satisfactory to Landlord protecting Landlord and the Condominium Board against liability for personal injury or property damage during construction. Upon completion of any Alterations, Tenant shall deliver to Landlord: (i) sworn statements setting forth the names of all contractors and subcontractors who did the work and final lien waivers from all such contractors and subcontractors; and (ii) "as built" plans for any such Alteration.

(d) Other than (i) the items, if any, listed on **Exhibit F** attached hereto, (ii) any items agreed by Landlord in writing to be included on **Exhibit F** in the future, and (iii) any trade fixtures, machinery, equipment and other personal property which may be removed without damage to the Premises, which damage shall be repaired (including capping or terminating utility hook-ups behind walls) by Tenant prior to the expiration or earlier termination of the Term (collectively, "**Tenant's Property**"), all property of any kind paid for by or on behalf of Landlord, all Alterations, real property fixtures, built-in machinery and equipment, built-in casework and cabinets and other similar additions and improvements built into the Premises so as to become an integral part of the Premises such as fume hoods which penetrate the roof or plenum area, built-in cold rooms, built-in warm rooms, walk-in cold rooms, walk-in warm rooms, deionized water systems, glass washing equipment, autoclaves, chillers, built-in plumbing, electrical and mechanical equipment and systems, and any power generator and transfer switch (collectively, "**Installations**") shall be and shall remain the property of Landlord during the Term and following the expiration or earlier termination of the Term, shall not be removed by Tenant at any time during the Term and shall remain upon and be surrendered with the Premises as a part thereof in accordance with Section 28 following the expiration or earlier termination of this Lease; provided, however, that Landlord shall, at the time its approval of such Installation is requested notify Tenant if it has elected to cause Tenant to remove such Installation upon the expiration or earlier termination of this Lease. If Landlord so elects, Tenant shall remove such Installation upon the expiration or earlier termination of this Lease and restore any damage caused by or occasioned as a result of such removal, including, when removing any of Tenant's Property which was plumbed, wired or otherwise connected to any of the Building Systems, capping off all such connections behind the walls of the Premises and repairing any holes. In the event Tenant fails to remove any

such Installation in accordance with the foregoing sentence, Landlord may do so at Tenant's expense. During any such restoration period that extends beyond the expiration or earlier termination of the Term, Tenant shall pay Rent to Landlord as provided herein as if said space were otherwise occupied by Tenant.

(e) No Alteration shall (i) affect the exterior walls, fascia or fenestration of the Building or the demising walls of the Premises, (ii) affect any part of the Project other than the Premises or require any alterations, installations, improvements, additions or other physical changes to be performed in or made to any portion of the Project other than the Premises, (iii) adversely affect any service required to be furnished by Landlord to Tenant or to any other tenant or occupant of the Project, (iv) adversely affect the functioning of any Building System, and (v) affect or require an amendment to (other than to confirm completion of the Alteration) the Certificate of Occupancy for the Premises or for any other part of the Project.

(f) Tenant covenants and agrees that no security agreement, lien, lease, conditional sales agreement, chattel mortgage or other title retention or instrument of similar import (a "**Security Agreement**") shall be placed upon any improvement made by Tenant which is affixed to the Premises. In the event that any of Tenant's Property are purchased or acquired by Tenant subject to a Security Agreement, Tenant agrees that no Security Agreement or Uniform Commercial Code filing statement shall be permitted to be filed against the Premises, the Building or any other part of the Project. If any such lien, based on a Security Agreement or Uniform Commercial Code filing statement, is filed against the Premises or any other part of the Project, Tenant shall, within 20 business days following notice thereof from Landlord, cause such lien or notice to be removed or discharged at Tenant's cost and expense.

(g) Tenant shall use its commercially reasonable and diligent efforts to perform such Alterations and other work at such times and in such manner as shall minimize any interference, disruption or disturbance from such performance.

(h) Tenant shall not, at any time prior to or during the Term, directly or indirectly employ, or permit the employment of, any contractor, mechanic or laborer in the Premises, in connection with any Alteration, if such employment would interfere or cause any conflict with other contractors, mechanics or laborers engaged in the construction, maintenance or operation of the Project by Landlord, Tenant or others. In the event of any such interference or conflict, Tenant, upon demand of Landlord, shall cause all contractors, mechanics or laborers causing such interference or conflict to leave the Building immediately.

13. **Landlord's Repairs.** Landlord, as an Operating Expense, shall maintain all of the structural and Building Systems (as defined below) in good repair, reasonable wear and tear and uninsured losses and damages caused by Tenant, or by any of Tenant's agents, servants, employees, invitees and contractors (collectively, "**Tenant Parties**") excluded. Losses and damages caused by Tenant or any Tenant Party shall be repaired by Landlord at Tenant's sole cost and expense. Landlord reserves the right to stop Building Systems services when necessary (i) by reason of accident or emergency, or (ii) for planned repairs, alterations or improvements, which are, in the judgment of Landlord, desirable or necessary to be made, until said repairs, alterations or improvements shall have been completed. Landlord shall have no responsibility or liability for failure to supply Building Systems services during any such period of interruption; provided,

however, that Landlord shall, except in case of emergency, make a commercially reasonable effort to give Tenant 24 hours advance notice of any planned stoppage of Building Systems services for routine maintenance, repairs, alterations or improvements. Tenant shall promptly give Landlord written notice of any repair required to be effected by Landlord pursuant to this Section 13, after which Landlord shall have a reasonable opportunity to effect such repair. Landlord shall not be liable for any failure to make any repairs or to perform any maintenance unless such failure shall persist for an unreasonable time after Tenant's written notice of the need for such repairs or maintenance. Tenant waives its rights under any state or local law to terminate this Lease or to make such repairs at Landlord's expense and agrees that the parties' respective rights with respect to such matters shall be solely as set forth herein. Repairs required as the result of fire, earthquake, flood, vandalism, war, or similar cause of damage or destruction shall be controlled by Section 18. As used herein, the term "**Building Systems**" shall mean, collectively, the HVAC, plumbing, fire sprinkler, elevators and all other building systems located outside of the Premises and serving the Premises and other portions of the Project,

If at any time any windows of the Premises are temporarily closed or darkened due to any Legal Requirement or by reason of repairs, maintenance, alterations, or improvements to the Building, or any scaffolding or "sidewalk bridge" is erected in front of the Building due to any Legal Requirement or by reason of any repairs, maintenance, alterations to the Building or any property adjacent to the Building, Landlord shall not be liable for any damage Tenant may sustain thereby and Tenant shall not be entitled to any compensation therefor, nor abatement or diminution of Base Rent or any other amount due under this Lease, nor shall the same release Tenant from its obligations hereunder, in whole or in part, by reason of inconvenience or annoyance to Tenant, or injury to or interruption of Tenant's business, or otherwise, nor impose any liability upon Landlord or its agents.

14. **Tenant's Repairs.** Subject to Section 13 hereof, Tenant, at its expense, shall repair, replace and maintain in good condition all portions of the Premises, including, without limitation, entries, doors, ceilings, interior windows, interior walls, and the interior side of demising walls. Such repair and replacement may include capital expenditures and repairs whose benefit may extend beyond the Term. Should Tenant fail to make any such repair or replacement or fail to maintain the Premises, Landlord shall give Tenant notice of such failure. If Tenant fails to commence cure of such failure within 10 days of Landlord's notice, and thereafter diligently prosecute such cure to completion, Landlord may perform such work and shall be reimbursed by Tenant within 10 days after demand therefor; provided, however, that if such failure by Tenant creates or could create an emergency, Landlord may immediately commence cure of such failure and shall thereafter be entitled to recover the costs of such cure from Tenant. Subject to Sections 17 and 18, Tenant shall bear the full uninsured cost of any repair or replacement to any part of the Project that results from damage caused by Tenant or any Tenant Party and any repair that benefits only the Premises. Tenant shall not clean nor require, permit, suffer or allow any window in the Premises to be cleaned from the outside in violation of Section 202 of New York State Labor Law or any other applicable law, or of the Rules of the Board of Standards and Appeals, or of any other Board or body having or asserting jurisdiction.

15. **Mechanic's Liens.** Tenant shall discharge, by bond or otherwise, any mechanic's lien filed against the Premises or against the Project for work claimed to have been done for, or materials claimed to have been furnished to, Tenant (other than for Landlord's Work) within 10

days after the filing thereof, at Tenant's sole cost and shall otherwise keep the Premises and the Project free from any liens arising out of work performed for, materials furnished to, or obligations incurred by Tenant. Should Tenant fail to discharge any lien described herein, Landlord shall have the right, but not the obligation, to pay such claim or post a bond or otherwise provide security to eliminate the lien as a claim against title to the Project and the cost thereof shall be immediately due from Tenant as Additional Rent. If Tenant shall lease or finance the acquisition of office equipment, furnishings, or other personal property of a removable nature utilized by Tenant in the operation of Tenant's business, Tenant covenants that any Security Agreement, and any Uniform Commercial Code Financing Statement filed as a matter of public record by any lessor or creditor of Tenant, shall upon its face or by exhibit thereto indicate that such Security Agreement or Financing Statement is applicable only to removable personal property of Tenant located within the Premises. Tenant shall cause to be inserted in any such Security Agreement the following provision: "Notwithstanding anything to the contrary contained herein, this lease, chattel mortgage, conditional sales agreement, title retention agreement or security agreement shall not create or be filed as a lien against the land, building and improvements comprising the real property in which the goods, machinery, equipment, appliances or other personal property covered hereby are to be located or installed"; and, in no event shall the address of the Project be furnished on any such Financing Statement without qualifying language as to applicability of the lien only to removable personal property, located in an identified suite held by Tenant.

16. **Indemnification.** Tenant shall indemnify, defend and hold harmless Landlord and the Condominium Board, the entities (if any) comprising Landlord, each affiliate or subsidiary of Landlord, and its and their partners, members, shareholders, officers, directors, employees and agents, Lessors (including, without limitation, the City and any administrator of the Ground Lease) and Mortgagees (as defined in Section 27) (each individually and collectively the "**Landlord Indemnitees**") from and against any and all Claims against the Landlord Indemnitees of whatever nature arising directly or indirectly from, or out of: (a) any negligence or willful misconduct by, Tenant, its officers, members, managers, directors, partners, contractors, licensees, agents, servants, employees, invitees or visitors, sublessees and assigns (b) any accident, injury, death or damage whatsoever caused to any Person or to the property of any Person occurring within or about the Premises, (c) any accident, injury, death or damage whatsoever caused to any Person or to the property of any Person occurring outside of the Premises but anywhere within or about the Land, where such accident, injury, death or damage is caused (or is claimed to have been caused) by or otherwise involves an act or omission, or the negligence or willful misconduct, of Tenant or Tenant's contractors, licensees, agents, servants, employees, invitees or visitors and (d) any accident, injury, death or damage whatsoever caused to any Person or to the property of any Person occurring within or about the Premises, where such accident, injury, death or damage is caused (or is claimed to have been caused) by or otherwise relates to the use or occupancy of the Premises or a breach or default by Tenant in the performance of any of its obligations hereunder, unless, in each case set forth in clauses (a) through (d), caused solely by the willful misconduct or negligence of Landlord. This indemnity, defense and hold harmless agreement shall include indemnification from and against any and all liability, fines, suits, demands, costs and expenses of any kind or nature (including reasonable attorneys' fees and disbursements) incurred in or in connection with any such claim or proceeding brought thereon, and the defense thereof.

## 17. Insurance.

(a) Landlord shall maintain all risk property and, if applicable, sprinkler damage insurance covering the full replacement cost of the Project or such lesser coverage amount as Landlord may elect provided such coverage amount is not less than 90% of such full replacement cost. Landlord shall further procure and maintain commercial general liability insurance with a single loss limit of not less than \$2,000,000 for bodily injury and property damage with respect to the Project. Landlord may, but is not obligated to, maintain such other insurance and additional coverages as it may deem necessary, including, but not limited to, flood, environmental hazard and earthquake, loss or failure of building equipment, errors and omissions, rental loss during the period of repair or rebuilding, workers' compensation insurance and fidelity bonds for employees employed to perform services and insurance for any improvements installed by Tenant or which are in addition to the standard improvements customarily furnished by Landlord without regard to whether or not the same are made a part of the Project. All such insurance, including any deductible associated therewith, shall be included as part of the Operating Expenses. The Project may be included in a blanket policy (in which case the cost of such insurance allocable to the Project will be determined by Landlord and/or the Condominium Board based upon the insurer's cost calculations). Tenant shall also reimburse Landlord for any increased premiums or additional insurance which Landlord reasonably deems necessary as a result of Tenant's use of the Premises. Tenant (and, during the prosecution of any Alterations, its general contractor, contractors and/or subcontractors), at its sole cost and expense, shall maintain during the Term: all risk property insurance (including fire, extended coverage, vandalism, boiler and machinery (and artificially generated electrical current), water and sprinkler damage, and off-premises failure of power or other utility services) with 18 months of business interruption and extra expense coverage, covering the full replacement cost of all property and improvements installed or placed in the Premises by Tenant at Tenant's expense (including, without limitation, builder's risk coverage for all Alterations); workers' compensation insurance with no less than the minimum limits required by law; employer's liability insurance with such limits as required by law; comprehensive automobile liability insurance (including automotive liability, including pollution coverage, from loading and unloading) with combined bodily injury and property damage coverage limits, per occurrence, of at least \$1,000,000; and commercial general liability insurance and umbrella liability, in each case, for minimum combined bodily injury and property damage coverage limits totaling \$2,000,000 per occurrence and \$5,000,000 in the aggregate. The commercial general liability insurance policy shall name (i) Landlord, (ii) its officers, members, shareholders, directors, employees, managers, agents, invitees, contractors, subcontractors, general contractor (or construction manager, as applicable), (iii) Alexandria Real Estate Equities, Inc., (iv) New York City Health and Hospitals Corporation (and any other Ground Landlord (as defined in Section 27) from time to time), (v) the City, (vi) the IDA (as defined in Section 27), (vii) the New York City Economic Development Corporation (and any other Ground Lease (as defined in Section 27) administrator/agent from time to time), and (viii) the Condominium Board (collectively, "**Landlord Parties**"), as additional insureds, the specific entities which are to be named are set forth in **Exhibit J** hereto; insure on an occurrence and not a claims-made basis; be issued by insurance companies which have a rating of not less than policyholder rating of A and financial category rating of at least Class X in "Best's Insurance Guide"; shall not be cancelable for nonpayment of premium unless 30 days prior written notice shall have been given to Landlord and the Condominium Board from the insurer; contain a hostile fire endorsement and a contractual liability endorsement; and provide primary coverage to Landlord and the Condominium Board

(any policy issued to Landlord or the Condominium Board providing duplicate or similar coverage shall be deemed excess over Tenant's policies). Copies of such policies (if requested by Landlord or the Condominium Board), or certificates of insurance showing the limits of coverage required hereunder and showing Landlord and the Condominium Board as an additional insured, along with reasonable evidence of the payment of premiums for the applicable period, shall be delivered to Landlord and the Condominium Board by Tenant upon commencement of the Term and prior to or upon each renewal of said insurance. Tenant's policy may be a "blanket policy" with an aggregate per location endorsement which specifically provides that the amount of insurance shall not be prejudiced by other losses covered by the policy. Tenant shall, at least 5 business days prior to the expiration of such policies, furnish Landlord and the Condominium Board with renewal certificates. In addition, upon receipt by Tenant of any notice of cancellation or any other notice from the insurance carrier which may adversely affect the coverage of the insureds under such policy of insurance, Tenant shall promptly deliver to Landlord and the Condominium Board and any other additional insured hereunder a copy of such notice. If at any time Tenant (or its general contractor, contractors and/or subcontractors) shall fail to procure or maintain all insurance required to be carried by Tenant pursuant to this Lease, Landlord or the Condominium Board may procure (but shall have no obligation to procure) such insurance on behalf of Tenant (and its general contractor, contractors and/or subcontractors) and the cost thereof shall be payable by Tenant upon demand. Such insurer(s) shall be selected by Tenant, subject to Landlord's approval, not to be unreasonably withheld, conditioned or delayed.

(b) In each instance where insurance is to name Landlord and the Condominium Board as an additional insured, Tenant shall upon written request of Landlord also designate and furnish certificates so evidencing Landlord and the Condominium Board as additional insured to: (i) any lender of Landlord or the Condominium Board holding a security interest in the Project or any portion thereof, (ii) the landlord under any lease wherein Landlord is tenant of the real property on which the Project is located, if the interest of Landlord is or shall become that of a tenant under a ground or other underlying lease rather than that of a fee owner, and/or (iii) any management company retained by Landlord or the Condominium Board to manage the Project.

(c) The property insurance obtained by Landlord and Tenant shall include a waiver of subrogation by the insurers and all rights based upon an assignment from its insured, against Landlord or Tenant, and their respective officers, directors, employees, members, managers, shareholders, partners, agents, representatives, servants, guests, invitees, visitors and contractors ("**Related Parties**"), in connection with any loss or damage thereby insured against. The Condominium Board shall also be a Related Party of Landlord hereunder. Neither party nor its respective Related Parties shall be liable to the other for loss or damage caused by any risk insured against under property insurance required to be maintained hereunder, and each party waives any claims against the other party, and its respective Related Parties, for such loss or damage. The failure of a party to insure its property shall not void this waiver. Landlord and its respective Related Parties shall not be liable for, and Tenant hereby waives all claims against such parties for, business interruption and losses occasioned thereby sustained by Tenant or any person claiming through Tenant resulting from any accident or occurrence in or upon the Premises or the Project from any cause whatsoever. If the foregoing waivers shall contravene any law with respect to exculpatory agreements, the liability of Landlord or Tenant shall be deemed not released but shall be secondary to the other's insurer.



(d) Landlord may require insurance policy limits to be raised to conform with requirements of Landlord's lender or the Condominium Board and/or to bring coverage limits to levels then being generally required of new tenants within the Project.

(e) Tenant acknowledges that Landlord shall not carry insurance on, and shall not be responsible for damage to, Tenant's Property or any Alterations, betterments or improvements made by Tenant to the Premises. Tenant agrees that Landlord shall not be required to maintain insurance coverage with respect to the portions of the Premises for which Tenant is required to maintain insurance in accordance with the terms of this Lease.

#### 18. Restoration.

(a) If, at any time during the Term, the Project or the Premises are damaged or destroyed by a fire or other insured casualty, Landlord shall notify Tenant within 60 days after discovery of such damage or destruction as to the amount of time Landlord reasonably estimates it will take to restore the Project or the Premises, as applicable (the "**Restoration Period**"). If the Restoration Period is estimated to exceed 12 months from the date that Landlord obtains all required permits to perform the restoration (the "**Maximum Restoration Period**"), Landlord may, in such notice, elect to terminate this Lease as of the date that is 75 days after the date of discovery of such damage or destruction. Unless Landlord so elects to terminate this Lease, Landlord shall, subject to receipt of sufficient insurance proceeds (with any deductible to be treated as a current Operating Expense), promptly restore the Premises (excluding any improvements installed by Tenant or by Landlord and paid for by Tenant unless covered by the insurance Landlord maintains as an Operating Expense hereunder, in which case such improvements shall be included, to the extent of such insurance proceeds, in Landlord's restoration), subject to delays arising from the collection of insurance proceeds, from Force Majeure events or as needed to obtain any license, clearance or other authorization of any kind required to enter into and restore the Premises issued by any Governmental Authority having jurisdiction over the use, storage, handling, treatment, generation, release, disposal, removal or remediation of Hazardous Materials (as defined in Section 30) in, on or about the Premises (collectively referred to herein as "**Hazardous Materials Clearances**"); provided, however, that if repair or restoration of the Premises is not substantially complete as of the end of the Maximum Restoration Period or, if longer, the Restoration Period, Landlord may, in its sole and absolute discretion, elect not to proceed with such repair and restoration, in which event Landlord shall be relieved of its obligation to make such repairs or restoration and this Lease shall terminate as of the date that is 75 days after the later of: (i) discovery of such damage or destruction, and (ii) the date all required Hazardous Materials Clearances are obtained, but Landlord shall retain any Rent paid and the right to any Rent payable by Tenant prior to such election by Landlord or Tenant.

(b) Tenant, at its expense, shall promptly perform, subject to delays arising from the collection of insurance proceeds, from Force Majeure (as defined in Section 34) events or from obtaining Hazardous Materials Clearances, all repairs or restoration not required to be done by Landlord and shall promptly re-enter the Premises and commence doing business in accordance with this Lease. Notwithstanding the foregoing, Landlord may terminate this Lease if the Premises are damaged during the last year of the Term and Landlord reasonably estimates that it will take more than 2 months to repair such damage, or if insurance proceeds are not available for such restoration. Rent shall be abated from the date all required Hazardous Material Clearances are

obtained until the repair and restoration of the Premises is substantially completed, in the proportion which the area of the Premises, if any, which is not usable by Tenant bears to the total area of the Premises, unless Landlord provides Tenant with other space during the period of repair that is suitable for the temporary conduct of Tenant's business. Such abatement shall be the sole remedy of Tenant, and except as provided in this Section 18, Tenant waives any right to terminate this Lease by reason of damage or casualty loss.

(c) The provisions of this Lease, including this Section 18, constitute an express agreement between Landlord and Tenant with respect to any and all damage to, or destruction of, all or any part of the Premises, or any other portion of the Project, and any statute or regulation which is now or may hereafter be in effect shall have no application to this Lease or any damage or destruction to all or any part of the Premises or any other portion of the Project, the parties hereto expressly agreeing that this Section 18 sets forth their entire understanding and agreement with respect to such matters.

(d) Tenant hereby expressly waives the provision of Section 227 of the Real Property Law and agrees that the foregoing provisions of this Section 18 shall govern and control in lieu thereof, this Section 18 being an express agreement.

(e) Landlord and Tenant acknowledge that Condominium Board has the responsibility under the Condominium By-Laws for certain aspects of restoration. In the event that Condominium Board, not Landlord, is responsible, in part or in full, under the Condominium Declaration for a restoration under this Section 18, the fulfillment by the Condominium Board of such obligation of Landlord, in part or in full, shall be deemed to constitute satisfaction by Landlord to the same extent of the restoration obligations of Landlord hereunder.

19. **Condemnation.** If the whole or any material part of the Premises, the Building or the Project is taken for any public or quasi-public use under governmental law, ordinance, or regulation, or by right of eminent domain, or by private purchase in lieu thereof (a "**Taking**" or "**Taken**"), and the Taking would in Landlord's reasonable judgment, either prevent or materially interfere with Tenant's use of the Premises or materially interfere with or impair Landlord's ownership or operation of the Building or Project, then upon written notice by Landlord this Lease shall terminate and Rent shall be apportioned as of said date. If part of the Premises shall be Taken, and this Lease is not terminated as provided above, Landlord shall promptly restore the Premises and the Project as nearly as is commercially reasonable under the circumstances to their condition prior to such partial Taking and the rentable square footage of the Building, the rentable square footage of the Premises, Tenant's Share of Operating Expenses and the Rent payable hereunder during the unexpired Term shall be reduced to such extent as may be fair and reasonable under the circumstances. Upon any such Taking, Landlord shall be entitled to receive the entire price or award from any such Taking without any payment to Tenant, and Tenant hereby assigns to Landlord Tenant's interest, if any, in such award. Tenant shall have the right, to the extent that same shall not diminish Landlord's award, to make a separate claim against the condemning authority (but not Landlord) for such compensation as may be separately awarded or recoverable by Tenant for moving expenses and damage to Tenant's trade fixtures, if a separate award for such items is made to Tenant. Tenant hereby waives any and all rights it might otherwise have pursuant to any provision of state law to terminate this Lease upon a partial Taking of the Premises or the Project.

20. **Events of Default.** Each of the following events shall be a default (“**Default**”) by Tenant under this Lease:

(a) **Payment Defaults.** Tenant shall fail to pay any installment of Rent or any other payment hereunder when due, including, without limitation, any penalties or interest accrued thereon.

(b) **Insurance.** Any insurance required to be maintained by Tenant pursuant to this Lease shall be canceled or terminated or shall expire or shall be reduced or materially changed, or Landlord or the Condominium Board shall receive a notice of nonrenewal of any such insurance and Tenant shall fail to obtain replacement insurance at least 20 days before the expiration, cancellation, termination, or reduction of, or material change in, the current coverage.

(c) **Abandonment.** Tenant shall abandon the Premises.

(d) **Improper Transfer.** Tenant shall assign, sublease or otherwise transfer (including, without limitation, by operation of law) or attempt to transfer all or any portion of Tenant’s interest in this Lease or the Premises except as expressly permitted herein, or Tenant’s interest in this Lease shall be attached, executed upon, or otherwise judicially seized and such action is not released or dismissed within 90 days of the action.

(e) **Liens.** Tenant shall fail to discharge or otherwise obtain the release of any lien placed upon the Premises in violation of this Lease within 10 days after any such lien is filed against the Premises.

(f) **Insolvency Events.** Tenant or any guarantor or surety of Tenant’s obligations hereunder shall: (A) make a general assignment for the benefit of creditors; (B) commence any case, proceeding or other action seeking to have an order for relief entered on its behalf as a debtor or to adjudicate it a bankrupt or insolvent, or seeking reorganization, arrangement, adjustment, liquidation, dissolution or composition of it or its debts or seeking appointment of a receiver, trustee, custodian or other similar official for it or for all or of any substantial part of its property (collectively a “**Proceeding for Relief**”); (C) become the subject of any Proceeding for Relief which is not dismissed within 90 days of its filing or entry or (D) die or suffer a legal disability (if Tenant, guarantor, or surety is an individual) or be dissolved or otherwise fail to maintain its legal existence (if Tenant, guarantor or surety is a corporation, partnership or other entity).

(g) **Estoppel Certificate or Subordination Agreement.** Tenant fails to execute any document required from Tenant under Sections 23 or 27 within 5 days after a second notice requesting such document.

(h) **Other Defaults.** Tenant shall fail to observe, perform or comply with any provision of this Lease other than those specifically referred to in this Section 20, and, except as otherwise expressly provided herein, such failure shall continue for a period of 10 days after written notice thereof from Landlord to Tenant.

Any notice given under Section 20(h) hereof shall: (i) specify the alleged default, (ii) demand that Tenant cure such default, (iii) be in lieu of, and not in addition to, or shall be deemed to be, any notice required under any provision of applicable law, and (iv) not be deemed a forfeiture or a

termination of this Lease unless Landlord elects otherwise in such notice; provided that if the nature of Tenant's default pursuant to Section 20(h) is such that it cannot be cured by the payment of money and reasonably requires more than 10 days to cure, then Tenant shall not be deemed to be in default if Tenant commences such cure within said 10 day period and thereafter diligently prosecutes the same to completion; provided, however, that such cure shall be completed no later than 30 days from the date of Landlord's notice.

## 21. Landlord's Remedies.

(a) **Payment By Landlord; Interest.** Upon a Default by Tenant hereunder, Landlord may, without waiving or releasing any obligation of Tenant hereunder, make such payment or perform such act. All sums so paid or incurred by Landlord, together with interest thereon (from the date such sums were paid or incurred, at the annual rate (the "**Default Rate**") equal to the Prime Rate + 4% (but in no event less than 12% or more than the maximum rate permitted under applicable law)) shall be payable to Landlord on demand as additional Rent. Nothing herein shall be construed to create or impose a duty on Landlord to mitigate any damages resulting from Tenant's Default hereunder. As used herein, the term "**Prime Rate**" shall mean the highest prime rate (or base rate) reported in the Money Rates column or section of The Wall Street Journal (Eastern Edition) published from time to time, as the rate in effect for corporate loans at large U.S. money center commercial banks (whether or not such rate has actually been charged by any such bank). If The Wall Street Journal ceases publication of the Prime Rate, the "Prime Rate" shall mean the prime rate (or base rate) announced by Citibank, N.A., New York, New York (whether or not such rate has actually been charged by such bank). If such bank discontinues the practice of announcing the Prime Rate, the "Prime Rate" shall mean the highest rate charged by such bank on short-term, unsecured loans to its most creditworthy large corporate borrowers.

(b) **Late Payment Rent.** Late payment by Tenant to Landlord of Rent and other sums due will cause Landlord to incur costs not contemplated by this Lease, the exact amount of which will be extremely difficult and impracticable to ascertain. Such costs include, but are not limited to, processing and accounting charges and late charges which may be imposed on Landlord under any Mortgage covering the Premises. Therefore, if any installment of Rent due from Tenant is not received by Landlord within 5 days after the date such payment is due, Tenant shall pay to Landlord an additional sum of 6% of the overdue Rent as a late charge. The parties agree that this late charge represents a fair and reasonable estimate of the costs Landlord will incur by reason of late payment by Tenant. In addition to the late charge, Rent not paid when due and remaining unpaid on the 5<sup>th</sup> day after it first became due shall bear interest at the Default Rate from the date it first became due until paid.

(c) **Remedies.** Upon and during the continuance of a Default, Landlord, at its option, without further notice or demand to Tenant, shall have in addition to all other rights and remedies provided in this Lease, at law or in equity, the option to pursue any one or more of the following remedies, each and all of which shall be cumulative and nonexclusive, without any notice or demand whatsoever. No cure, in whole or in part, of such Default by Tenant after Landlord has taken any action (beyond giving Tenant notice of such Default) to pursue any remedy provided for herein (including retaining counsel to file an action or otherwise pursue any remedies) shall in any way affect Landlord's right to pursue such remedy or any other remedy provided Landlord herein or under law or in equity, unless Landlord, in its sole discretion, elects to waive such Default.

(i) This Lease and the Term and estate hereby granted are subject to the limitation that whenever a Default shall have happened and be continuing, Landlord shall have the right, at its election, then or thereafter while any such Default shall continue and notwithstanding the fact that Landlord may have some other remedy hereunder or at law or in equity, to give Tenant written notice of Landlord's intention to terminate this Lease on a date specified in such notice, which date shall be not less than 5 days after the giving of such notice, and upon the date so specified, this Lease and the estate hereby granted shall expire and terminate with the same force and effect as if the date specified in such notice were the date hereinbefore fixed for the expiration of this Lease, and all right of Tenant hereunder shall expire and terminate, and Tenant shall be liable as hereinafter in this Section 21(c) provided. If any such notice is given, Landlord shall have, on such date so specified, the right of re-entry and possession of the Premises and the right to remove all persons and property therefrom and to store such property in a warehouse or elsewhere at the risk and expense, and for the account, of Tenant. Should Landlord elect to re-enter as herein provided or should Landlord take possession pursuant to legal proceedings or pursuant to any notice provided for by law, Landlord may from time to time re-let the Premises or any part thereof for such term or terms and at such rental or rentals and upon such terms and conditions as Landlord may deem advisable, with the right to make commercially reasonable alterations in and repairs to the Premises.

(ii) In the event of any termination of this Lease as in this Section 21 provided or as required or permitted by law or in equity, Tenant shall forthwith quit and surrender the Premises to Landlord, and Landlord may, without further notice, enter upon, re-enter, possess and repossess the same by summary proceedings, ejectment or otherwise, and again have, repossess and enjoy the same as if this Lease had not been made, and in any such event neither Tenant nor any person claiming through or under Tenant by virtue of any law or an order of any court shall be entitled to possession or to remain in possession of the Premises. Landlord, at its option, notwithstanding any other provision of this Lease, shall be entitled to recover from Tenant, as and for liquidated damages, the sum of;

(A) all Base Rent, Additional Rent and other amounts payable by Tenant hereunder then due or accrued and unpaid; and

(B) the amount equal to the aggregate of all unpaid Base Rent and Additional Rent which would have been payable if this Lease had not been terminated prior to the end of the Term then in effect, discounted to its then present value in accordance with accepted financial practice using a rate of 5% per annum, for loss of the bargain; and

(C) all other damages and expenses (including attorneys' fees and expenses), if any, which Landlord shall have sustained by reason of the breach of any provision of this Lease; less

(D) the net proceeds of any re-letting actually received by Landlord.

(iii) Nothing herein contained shall limit or prejudice the right of Landlord, in any bankruptcy or insolvency proceeding, to prove for and obtain as liquidated damages by reason of such termination an amount equal to the maximum allowed by any bankruptcy or insolvency proceedings, or to prove for and obtain as liquidated damages by reason of such termination, an amount equal to the maximum allowed by any statute or rule of law whether such amount shall be greater or less than the excess referred to above.

(iv) Nothing in this Section 21 shall be deemed to affect the right of either party to indemnifications pursuant to this Lease.

(v) If Landlord terminates this Lease upon the occurrence of a Default, Tenant will quit and surrender the Premises to Landlord or its agents, and Landlord may, without further notice, enter upon, re-enter and repossess the Premises by summary proceedings, ejectment or otherwise. The words "enter", "re-enter", and "re-entry" are not restricted to their technical legal meanings.

(vi) If either party shall be in default in the observance or performance of any provision of this Lease, and an action shall be brought for the enforcement thereof in which it shall be determined that such party was in default, the party in default shall pay to the other all fees, costs and other expenses which may become payable as a result thereof or in connection therewith, including attorneys' fees and expenses.

(vii) If Tenant shall default in the keeping, observance or performance of any covenant, agreement, term, provision or condition herein contained, Landlord, without thereby waiving such default, may perform the same for the account and at the expense of Tenant (a) immediately or at any time thereafter and without notice in the case of emergency or in case such default will result in a violation of any legal or insurance requirements, or in the imposition of any lien against all or any portion of the Premises, and (b) in any other case if such default continues after any applicable cure period provided in Section 20. All reasonable costs and expenses incurred by Landlord and/or the Condominium Board in connection with any such performance by it for the account of Tenant and all reasonable costs and expenses, including attorneys' fees and disbursements incurred by Landlord and/or the Condominium Board in any action or proceeding (including any summary dispossess proceeding) brought by Landlord and/or the Condominium Board to enforce any obligation of Tenant under this Lease and/or the right of Landlord and/or the Condominium Board in or to the Premises, shall be paid by Tenant to Landlord within 10 days after demand.

(viii) Independent of the exercise of any other remedy of Landlord hereunder or under applicable law, Landlord may conduct an environmental test of the Premises as generally described in Section 30(d), at Tenant's expense.

(ix) Nothing contained in this Lease shall be construed as limiting or precluding the recovery by Landlord against Tenant of any sums or damages to which, in addition to the damages particularly provided above, Landlord may lawfully be entitled by reason of any default hereunder on the part of Tenant. Anything in this Lease to the contrary notwithstanding, during the continuation of any default by Tenant, Tenant shall not be entitled to exercise any rights or options, or to receive any funds or proceeds being held, under or pursuant to this Lease.

(x) Tenant waives and surrenders all right and privilege that Tenant might have under or by reason of any present or future law to redeem the Premises or to have a continuance of this Lease after Tenant is dispossessed or ejected therefrom by process of law or under the terms

of this Lease or after any termination of this Lease. Tenant also waives the provisions of any law relating to notice and/or delay in levy of execution in case of any eviction or dispossession for nonpayment of rent, and the provisions of any successor or other law of like import.

(xi) Except as otherwise provided in this Section 21, no right or remedy herein conferred upon or reserved to Landlord is intended to be exclusive of any other right or remedy, and every right and remedy shall be cumulative and in addition to any other legal or equitable right or remedy given hereunder, or now or hereafter existing. No waiver of any provision of this Lease shall be deemed to have been made unless expressly so made in writing. Landlord shall be entitled, to the extent permitted by law, to seek injunctive relief in case of the violation, or attempted or threatened violation, of any provision of this Lease, or to seek a decree compelling observance or performance of any provision of this Lease, or to seek any other legal or equitable remedy.

(xii) Landlord may continue to collect Rent as the same becomes due without terminating this Lease and without waiving any other rights or remedies Landlord may have.

(xiii) Anything contained herein to the contrary notwithstanding, if any termination of this Lease shall be stayed by order of any court having jurisdiction over any proceeding related to an insolvency event described herein, or by federal or state statute, then, following the expiration of any such stay, or if the trustee appointed in any such proceeding, Tenant or Tenant as debtor-in-possession shall fail to assume Tenant's obligations under this Lease within the period prescribed therefor by law (or within 90 days after entry of the order for relief if no such period is prescribed by law) or such other period as may be allowed by the court, or if said trustee, Tenant or Tenant as debtor-in-possession shall fail to provide adequate protection of Landlord's right, title and interest in and to the Premises or adequate assurance of the complete and continuous future performance of Tenant's obligations under this Lease, Landlord, to the extent permitted by law or by leave of the court having jurisdiction over such proceeding, shall have the right, at its election, to terminate this Lease on 5 days' notice to Tenant, Tenant as debtor-in-possession or said trustee and upon the expiration of said 5 day period this Lease shall cease and expire as aforesaid and Tenant, Tenant as debtor-in-possession or said trustee shall promptly quit and surrender the Premises as aforesaid.

(xiv) Except as expressly provided herein, none of Landlord or any Landlord Party shall be liable for consequential damages hereunder.

## 22. **Assignment and Subletting.**

(a) **General Prohibition.** Without Landlord's prior written consent subject to and on the conditions described in this Section 22, Tenant shall not, directly or indirectly, voluntarily or by operation of law, assign this Lease or sublease the Premises or any part thereof or mortgage, pledge, or hypothecate its leasehold interest or grant any concession or license within the Premises, and any attempt to do any of the foregoing shall be void and of no effect. If Tenant is a corporation, partnership or limited liability company, the shares or other ownership interests thereof which are not actively traded upon a stock exchange or in the over-the-counter market, a transfer or series of related or unrelated transfers whereby twenty-five percent (25%) or more of the issued and outstanding shares or other direct or indirect ownership interests of such corporation, partnership or limited liability company are, or voting control is, transferred (but excepting transfers upon

deaths of individual owners) from a person or persons or entity or entities which were owners thereof at the time of execution of this Lease to persons or entities who were not owners of at least fifty percent (50%) of the shares or other ownership interests of the corporation, partnership or limited liability company at the time of execution of this Lease, shall be deemed an assignment of this Lease requiring the consent of Landlord as provided in this Section 22. Notwithstanding the foregoing, any public offering of shares or other ownership interest in Tenant on a recognized domestic U.S. stock exchange shall not be deemed an assignment.

(b) If this Lease is assigned to any person or entity pursuant to the provisions of 11 U.S.C. Section 101 et seq., or any successor statute (the "**Bankruptcy Code**"), any and all monies or other consideration payable or otherwise to be delivered in connection with such assignment shall be paid or delivered to Landlord, shall be and remain the exclusive property of Landlord and shall not constitute property of Tenant or of the estate of Tenant within the meaning of the Bankruptcy Code. Any and all monies or other consideration constituting Landlord's property under the preceding sentence not paid or delivered to Landlord shall be held in trust for the benefit of Landlord and shall be promptly paid to or turned over to Landlord.

(c) If Tenant desires to assign, hypothecate or otherwise transfer this Lease or to sublet the Premises other than pursuant to a Permitted Assignment (as defined below), then at least 15 business days, but not more than 45 business days, before the date Tenant desires the assignment or sublease to be effective (the "**Assignment Date**"), Tenant shall give Landlord a notice (the "**Assignment Notice**") containing such information about the proposed assignee or sublessee, including the proposed use of the Premises and any Hazardous Materials proposed to be used, stored, handled, treated, generated in or released or disposed of from the Premises, the Assignment Date, any relationship between Tenant and the proposed assignee or sublessee, and all material terms and conditions of the proposed assignment or sublease, including a copy of the proposed assignment or sublease in its final form, and such other information as Landlord may deem reasonably necessary or appropriate to its consideration as to whether to grant its consent. Landlord may, by giving written notice to Tenant within 15 business days after receipt of the Assignment Notice: (i) grant such consent, (ii) refuse such consent, in its sole and absolute discretion, if (A) the proposed assignment, hypothecation or other transfer or subletting concerns more than (together with all other then effective subleases) 50% of the Premises or (B) the proposed assignee or subtenant is a tenant of the Project or any other property owned (in whole or in part) or managed by Landlord or a subsidiary or affiliate of Landlord or any other Person that has, within the 6 months prior, initiated negotiations with Landlord regarding, or toured (or made an appointment to tour) the Project with a view to, letting any portion of the Project, (iii) refuse such consent, in its reasonable discretion, if the proposed subletting concerns (together with all other then effective subleases) 50% or less of the Premises (provided that Landlord shall further have the right to review and approve or disapprove the proposed form of sublease prior to the effective date of any such subletting), (iv) sublease such portion of the Premises from the Tenant on the terms described in the Assignment Notice., or (v) terminate this Lease with respect to the space described in the Assignment Notice as of the Assignment Date (an "**Assignment Termination**"). If Landlord delivers notice of its election to exercise an Assignment Termination, Tenant shall have the right to withdraw such Assignment Notice by written notice to Landlord of such election within 5 business days after Landlord's notice electing to exercise the Assignment Termination. If Tenant withdraws such Assignment Notice, this Lease shall continue in full force and effect. If Tenant does not withdraw such Assignment Notice, this Lease, and the term and estate herein granted,



shall terminate as of the Assignment Date with respect to the space described in such Assignment Notice. No failure of Landlord to exercise any such option to terminate this Lease, or to deliver a timely notice in response to the Assignment Notice, shall be deemed to be Landlord's consent to the proposed assignment, sublease or other transfer. Tenant shall reimburse Landlord for all of Landlord's reasonable out-of-pocket expenses in connection with its consideration of any Assignment Notice. Any Person to which this Lease is assigned pursuant to the provisions of the Bankruptcy Code shall be deemed without further act or deed to have assumed all of the obligations arising under this Lease on and after the date of such assignment.

(d) If Tenant assumes this Lease and proposes to assign the same pursuant to the provisions of the Bankruptcy Code to any Person who shall have made a bona fide offer to accept an assignment of this Lease on terms acceptable to Tenant, then notice of such proposed assignment shall be given to Landlord by Tenant no later than 20 days after receipt by Tenant, but in any event no later than 10 days prior to the date that Tenant shall make application to a court of competent jurisdiction for authority and approval to enter into such assignment and assumption. Such notice shall set forth (i) the name and address of such Person, (ii) all of the terms and conditions of such offer, and (iii) adequate assurance of future performance by such Person under the Lease as set forth below, including, without limitation, the assurance referred to in Section 365(b)(3) of the Bankruptcy Code. Landlord shall have the prior right and option, to be exercised by notice to Tenant given at any time prior to the effective date of such proposed assignment, to accept an assignment of this Lease upon the same terms and conditions and for the same consideration, if any, as the bona fide offer made by such Person, less any brokerage commissions which would otherwise be payable by Tenant out of the consideration to be paid by such Person in connection with the assignment of this Lease.

(e) The term "adequate assurance of future performance" as used in this Lease shall mean that any proposed assignee shall, among other things, (i) deposit with Landlord on the assumption of this Lease a sum equal to 12 monthly installments of the then Base Rent as security for the faithful performance and observance by such assignee of the terms and obligations of this Lease, (ii) furnish Landlord with financial statements of such assignee for the prior 3 fiscal years, as finally determined after an audit and certified as correct by a certified public accountant, which financial statements shall show (A) net annual operating income of at least 8 times the then annual Base Rent for each of such 3 years and (B) a net worth of at least 10 times the aggregate Base Rent payable during the remaining term of the Lease, (iii) grant to Landlord a security interest in such property of the proposed assignee as Landlord shall deem necessary to secure such assignee's future performance under this Lease, and (iv) provide such other information or take such action as Landlord, in its reasonable judgment shall determine is necessary to provide adequate assurance of the performance by such assignee of its obligations under this Lease.

(f) If, at any time after the originally named Tenant herein may have assigned Tenant's interest in this Lease, this Lease shall be disaffirmed or rejected in any insolvency proceeding of the types described herein, or in any similar proceeding, or in the event of termination of this Lease by reason of any such proceeding or by reason of lapse of time following notice of termination based upon any Event of Default, each prior Tenant, including, without limitation, the originally named Tenant, upon request of Landlord given within 30 days next following any such disaffirmance, rejection or termination (and actual notice thereof to Landlord in the event of a disaffirmance or rejection or in the event of termination other than by act of Landlord), shall (i)

pay to Landlord all Fixed Rent and other items of Rental due and owing by the assignee to Landlord under this Lease to and including the date of such disaffirmance, rejection or termination, and (ii) as "tenant", enter into a new lease with Landlord of the Premises for a term commencing on the effective date of such disaffirmance, rejection or termination and ending on the Expiration Date, unless sooner terminated as in such lease provided, at the same Fixed Rent and upon the then executory terms, covenants and conditions as are contained in this Lease, except that (A) Tenant's rights under the new lease shall be subject to the possessory rights of the assignee under this Lease and the possessory rights of any person claiming through or under such assignee or by virtue of any statute or of any order of any court, (B) such new lease shall require that Tenant shall cure all defaults existing under this Lease with due diligence, and (C) such new lease shall require Tenant to pay all items of Rental reserved in this Lease which, had this Lease not been so disaffirmed, rejected or terminated, would have accrued after the date of such disaffirmance, rejection or termination with respect to any period prior thereto. If any such prior Tenant shall default in its obligation to enter into said new lease for a period of 10 days next following Landlord's request therefor, then, in addition to all other rights and remedies by reason of such default, either at law or in equity, Landlord shall have the same rights and remedies against such Tenant as if such Tenant had entered into such new lease and such new lease had thereafter been terminated as of the commencement date thereof by reason of such Tenant's default thereunder.

Notwithstanding the foregoing, Landlord's consent to an assignment of this Lease or a subletting of any portion of the Premises to any Affiliate of Tenant (a "**Permitted Assignment**") shall not be required for so long as the transferee remains an Affiliate of Tenant and assumes all of the obligations of Tenant under this Lease, provided that Landlord shall have the right to approve the form of any such sublease or assignment.

(g) **Additional Conditions.** As a condition to any such assignment or subletting, whether or not Landlord's consent is required, Landlord may require:

(i) that any assignee or subtenant agree, in writing at the time of such assignment or subletting, that if Landlord gives such party notice that Tenant is in default under this Lease, such party shall thereafter make all payments otherwise due Tenant directly to Landlord, which payments will be received by Landlord without any liability except to credit such payment against those due under this Lease, and any such third party shall agree to attorn to Landlord or its successors and assigns should this Lease be terminated for any reason; provided, however, in no event shall Landlord or its successors or assigns be obligated to accept such attornment;

(ii) a list of Hazardous Materials, certified by the proposed assignee or sublessee to be true and correct, which the proposed assignee or sublessee intends to use, store, handle, treat, generate in, release or dispose of from the Premises, together with copies of all documents relating to such use, storage, handling, treatment, generation, release or disposal of Hazardous Materials by the proposed assignee or subtenant in the Premises or on the Project, prior to the proposed assignment or subletting, including, without limitation: permits; approvals; reports and correspondence; storage and management plans; plans relating to the installation of any storage tanks to be installed in or under the Project (provided, said installation of tanks shall only be permitted after Landlord has given its written consent to do so, which consent may be withheld in Landlord's sole and absolute discretion); and all closure plans or any other documents required

by any and all federal, state and local Governmental Authorities for any storage tanks installed in, on or under the Project for the closure of any such tanks. Neither Tenant nor any such proposed assignee or subtenant is required, however, to provide Landlord with any portion(s) of such documents containing information of a proprietary nature which, in and of themselves, do not contain a reference to any Hazardous Materials or hazardous activities;

(iii) that the originally named Tenant herein reaffirm its continuing primary liability under this Lease; and

(iv) that the assignee or subtenant remake the representations and warranties of Tenant hereunder as of the effective date of such assignment or subletting.

(h) **No Release of Tenant, Sharing of Excess Rents.** Notwithstanding any assignment or subletting, Tenant and any guarantor or surety of Tenant's obligations under this Lease shall at all times remain fully and primarily responsible and liable for the payment of Rent and for compliance with all of Tenant's other obligations under this Lease. If the Rent due and payable by a sublessee or assignee (or a combination of the rental payable under such sublease or assignment plus any bonus or other consideration therefor or incident thereto in any form) exceeds the rental payable under this Lease, (excluding however, any Rent payable under this Section 22) ("**Excess Rent**"), then Tenant shall be bound and obligated to pay Landlord as Additional Rent hereunder 50% of such Excess Rent within 10 days following receipt thereof by Tenant. If Tenant shall sublet the Premises or any part thereof, Tenant hereby immediately and irrevocably assigns to Landlord, as security for Tenant's obligations under this Lease, all rent from any such subletting, and Landlord as assignee and as attorney-in-fact for Tenant, or a receiver for Tenant appointed on Landlord's application, may collect such rent and apply it toward Tenant's obligations under this Lease; except that, until the occurrence of a Default, Tenant shall have the right to collect such rent.

(i) **No Waiver.** The consent by Landlord to an assignment or subletting shall not relieve Tenant or any assignees of this Lease or any sublessees of the Premises from obtaining the consent of Landlord to any further assignment or subletting nor shall it release Tenant or any assignee or sublessee of Tenant from full and primary liability under this Lease. The acceptance of Rent hereunder, or the acceptance of performance of any other term, covenant, or condition thereof, from any other person or entity shall not be deemed to be a waiver of any of the provisions of this Lease or a consent to any subletting, assignment or other transfer of the Premises.

(j) **Prior Conduct of Proposed Transferee.** Notwithstanding any other provision of this Section 22, if (i) the proposed assignee or sublessee of Tenant has been required by any prior landlord, lender or Governmental Authority to take remedial action in connection with Hazardous Materials contaminating a property, where the contamination resulted from such party's action or use of the property in question, (ii) the proposed assignee or sublessee is subject to an enforcement order issued by any Governmental Authority in connection with the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials (including, without limitation, any order related to the failure to make a required reporting to any Governmental Authority), or (iii) the risk that Landlord would be targeted as a responsible party in connection with the remediation of any pre-existing environmental condition in the vicinity of or underlying the Project would be materially increased or exacerbated by the proposed use of Hazardous Materials by such proposed assignee or sublessee, Landlord shall have the absolute right to refuse to consent to any assignment or subletting to any such party.

23. **Estoppel Certificate.** Tenant shall, within 10 business days of written notice from Landlord, execute, acknowledge and deliver a statement in writing in any form reasonably requested by a proposed lender or purchaser, (i) certifying that this Lease is unmodified and in full force and effect (or, if modified, stating the nature of such modification and certifying that this Lease as so modified is in full force and effect) and the dates to which the rental and other charges are paid in advance, if any, (ii) acknowledging that there are not any uncured defaults on the part of Landlord hereunder, or specifying such defaults if any are claimed, and (iii) setting forth such further information with respect to the status of this Lease or the Premises as may be requested thereon. Any such statement may be relied upon by any prospective purchaser or encumbrancer of all or any portion of the real property of which the Premises are a part. Tenant's failure to deliver such statement within such time shall, at the option of Landlord, be conclusive upon Tenant that the Lease is in full force and effect and without modification except as may be represented by Landlord in any certificate prepared by Landlord and delivered to Tenant for execution.

24. **Quiet Enjoyment.** So long as Tenant shall perform all of the covenants and agreements herein required to be performed by Tenant, Tenant shall, subject to the terms of this Lease and the Superior Instruments, at all times during the Term, have peaceful and quiet enjoyment of the Premises against any person claiming by, through or under Landlord.

25. **Prorations.** All prorations required or permitted to be made hereunder shall be made on the basis of a 360 day year and 30 day months.

26. **Rules and Regulations.** Tenant shall, at all times during the Term and any extension thereof, comply with all reasonable rules and regulations at any time or from time to time established by Landlord covering use of the Premises and the Project (the "**Rules and Regulations**"). The current Rules and Regulations are attached hereto as **Exhibit E**. If there is any conflict between said Rules and Regulations and other provisions of this Lease, the terms and provisions of this Lease shall control. Landlord shall not have any liability or obligation for the breach of any Rules or Regulations by other tenants in the Project and shall not enforce such Rules and Regulations in a discriminatory manner.

27. **Subordination.**

(a) The following capitalized terms, whenever used in this Lease, shall have the respective meanings ascribed to such terms as follows: (i) "**Superior Instruments**" shall mean each of the Ground Lease, the IDA Lease Documents, the Condominium Declaration and any Superior Lease or Mortgage, the Operating Agreement (as defined in the Ground Lease) and all matters to which any of the foregoing are subordinate; (ii) "**Ground Lease**" shall mean that certain Agreement of Lease, dated as of December 29, 2006, between New York City Health and Hospitals Corporation, a New York not-for-profit corporation, as landlord, and Landlord, as tenant, entered into in respect of the Project and as the same may be further amended or otherwise modified; (iii) "**Ground Landlord**" shall mean the then landlord under the Ground Lease; (iv) "**IDA Lease Documents**" shall mean, collectively, (A) that certain IDA Lease Agreement between Landlord, as landlord, and The New York City Industrial Development Agency ("**IDA**"), as tenant, dated as

of December 1, 2006, entered into in respect of the Project and as the same may be further amended or otherwise modified, and (B) that certain Lease Agreement (the "**IDA Lease**"), between IDA, as landlord, and Landlord as tenant, dated as of December 1, 2006 entered into in respect of the Project and as the same may be further amended or otherwise modified; (v) "**Superior Leases**" shall mean the leases to which this Lease is subject and subordinate; (vi) "**Superior Lessor**" shall mean the lessor under a Superior Lease; (vii) "**Superior Party**" shall mean each of the Ground Landlord, any Superior Lessor, the Condominium Board, any Mortgagee and the City of New York; (viii) "**Mortgage**" shall mean any mortgage, deed of trust, security assignment and other encumbrance now existing or hereafter created on or against the Project or the Premises, and all amendments, restatements, renewals, modifications, consolidations, refinancing, assignments and extensions thereof; (ix) "**Mortgagee**" shall mean the Holder or Holders (including the agent for any lending syndicate) of a Mortgage and shall be deemed to include the beneficiary under a deed of trust; and (x) the "**Condominium Declaration**" shall have the meaning set forth below.

On or about December 4, 2014, the Project was subjected to the provisions of Article 9-B of the New York Real Property Law, thereby creating The East River Science Park Condominium (the "**Condominium**") in accordance with that certain Declaration Establishing a Plan for Condominium Ownership of the Premises known as 430-450 East 29th Street, New York, New York Pursuant to Article 9-B of the Real Property Law of the State of New York, as the same may be further amended or otherwise modified (the "**Condominium Declaration**"). The units of the Condominium are sometimes referred to herein individually as a "**Unit**" and collectively as "**Units.**"

(b) This Lease and Tenant's interest and rights hereunder are hereby made and shall be subject and subordinate at all times to the Superior instruments and to the lien of any Mortgage, without the necessity of any further instrument or act on the part of Tenant; provided, however that so long as there is no Default hereunder, Tenant's right to possession of the Premises shall not be disturbed by the Holder of any such Mortgage. Tenant agrees, at the election of the Holder of any such Mortgage, to attorn to any such Holder. Tenant agrees upon demand to execute, acknowledge and deliver such instruments, confirming such subordination, and such instruments of attornment as shall be requested by any such Holder, provided any such instruments contain appropriate non-disturbance provisions assuring Tenant's quiet enjoyment of the Premises as set forth in Section 24 hereof. Tenant hereby appoints Landlord attorney-in-fact for Tenant irrevocably (such power of attorney being coupled with an interest) to execute, acknowledge and deliver any such instrument and instruments for and in the name of Tenant and to cause any such instrument to be recorded. Notwithstanding the foregoing, any such Holder may at any time subordinate its Mortgage to this Lease, without Tenant's consent, by notice in writing to Tenant, and thereupon this Lease shall be deemed prior to such Mortgage without regard to their respective dates of execution, delivery or recording and in that event such Holder shall have the same rights with respect to this Lease as though this Lease had been executed prior to the execution, delivery and recording of such Mortgage and had been assigned to such Holder. If (i) in connection with obtaining financing for the Project, or of any Superior Lease, or any modification to the Condominium Declaration, a banking, insurance or other Superior Party shall request reasonable modifications in this Lease as a condition to such financing or modification to the Condominium Declaration, and/or (ii) the provisions of any Superior Instruments require Tenant to deliver any instruments or acknowledgements, Tenant will not unreasonably withhold its consent thereto and/or unreasonably condition or delay the delivery thereof, as the case may be, provided that such

modifications and/or instruments or acknowledgements, in either instance, do not (A) extend or shorten the Term, (B) reduce the usable area of the Premises, (C) increase the Base Rent or any Additional Rent (D) except to a de minimis extent, otherwise increase the obligations of Tenant or the rights of Landlord under this Lease or (E) except to a de minimis extent, otherwise decrease the obligations of Landlord or the rights of Tenant under this Lease. At Ground Landlord's option, on the termination of the Ground Lease pursuant to an event of default by Landlord as the tenant thereunder, the Tenant shall attorn to, or shall enter into a direct lease on terms identical to the Lease with, Ground Landlord for the balance of the unexpired term of this Lease.

(c) By its execution and delivery of this Lease, Tenant expressly acknowledges and agrees that it shall comply, and cause its agents, employees, contractors, subcontractors, subtenants, operators, licensees, franchisees, concessionaires or other occupants of the Premises to comply, fully and faithfully at all times, to the extent applicable to the Premises, with all terms, covenants and conditions of the Superior Instruments of which Tenant has been given notice from time to time and which by their terms are applicable to a space lease of all or any portion of the Project (collectively, "**Tenant's Superior Instrument Obligations**"), such acknowledgment and agreement being a material inducement to Landlord's execution and delivery of this Lease and leasing of the Premises to Tenant. Tenant further acknowledges and agrees that, pursuant to the Ground Lease, any act or omission of Tenant or any of its agents, employees, contractors, subcontractors, subtenants, operators, licensees, franchisees, concessionaires or other occupants of the Premises that violates any provision of the Ground Lease may be deemed to be a violation of such provision by Landlord as the tenant under the Ground Lease.

(d) Tenant acknowledges and agrees that, notwithstanding anything herein to the contrary, Landlord may modify or amend this Lease from time to time in order to avoid the occurrence of a default under the Superior Instruments, provided such modification or amendment does not (i) extend or shorten the Term, (ii) reduce the usable area of the Premises, (iii) increase the Base Rent or any Additional Rent (iv) except to a de minimis extent, otherwise increase the obligations of Tenant or the rights of Landlord under this Lease or (v) except to a de minimis extent, otherwise decrease the obligations of Landlord or the rights of Tenant under this Lease. Tenant shall promptly execute any such modification or amendment to this Lease.

(e) The Condominium Board shall be a third party beneficiary of all sections in this Lease in which it is mentioned. In the event that, under the Condominium Documents, any duty of Landlord hereunder is within the power of the Condominium Board, (i) if Landlord and Condominium Board are Affiliates, such duty hereunder shall be a duty to cause Condominium Board to take such action, and (ii) if Landlord and Condominium Board are not Affiliates, such duty hereunder shall be a duty to take commercially reasonable efforts to cause Condominium Board to take such action. To the extent that Condominium Board shall fulfill any of Landlord's duties hereunder, the same shall constitute satisfaction by Landlord of such duties.

## 28. Surrender.

(a) Upon the expiration of the Term or earlier termination of Tenant's right of possession, Tenant shall surrender the Premises to Landlord in the same condition as received, subject to any Alterations or Installations permitted by Landlord to remain in the Premises, free of Hazardous Materials brought upon, kept, used, stored, handled, treated, generated in, or released

or disposed of from, the Premises by any person other than a Landlord Party (collectively, “**Tenant HazMat Operations**”) and with all Hazardous Materials Clearances in place, and in broom clean condition, ordinary wear and tear and casualty loss and condemnation (which are covered by Sections 18 and 19) excepted. At least 3 months prior to the surrender of the Premises, Tenant shall deliver to Landlord a narrative description of the actions proposed (or required by any Governmental Authority) to be taken by Tenant in order to surrender the Premises (including any Installations permitted by Landlord to remain in the Premises) at the expiration or earlier termination of the Term, free from any residual impact from the Tenant HazMat Operations and otherwise released for unrestricted use and occupancy (the “**Surrender Plan**”). Such Surrender Plan shall be accompanied by a current listing of (i) all Hazardous Materials licenses and permits held by or on behalf of any Tenant Party with respect to the Premises, and (ii) all Hazardous Materials used, stored, handled, treated, generated, released or disposed of from the Premises, and shall be subject to the review and approval of Landlord’s environmental consultant. In connection with the review and approval of the Surrender Plan, upon the request of Landlord, Tenant shall deliver to Landlord or its consultant such additional non-proprietary information concerning Tenant HazMat Operations as Landlord shall request. On or before such surrender, Tenant shall deliver to Landlord evidence that the approved Surrender Plan shall have been satisfactorily completed and Landlord shall have the right, subject to reimbursement at Tenant’s expense as set forth below, to cause Landlord’s environmental consultant to inspect the Premises and perform such additional procedures as may be deemed reasonably necessary to confirm that the Premises are, as of the effective date of such surrender or early termination of this Lease, free from any residual impact from Tenant HazMat Operations. Tenant shall reimburse Landlord, as Additional Rent, for the actual out-of-pocket expense incurred by Landlord for Landlord’s environmental consultant to review and approve the Surrender Plan and to visit the Premises and verify satisfactory completion of the same, which cost shall not exceed \$5,000. Landlord shall have the unrestricted right to deliver such Surrender Plan and any report by Landlord’s environmental consultant with respect to the surrender of the Premises to third parties.

(b) If Tenant shall fail to prepare or submit a Surrender Plan approved by Landlord, or if Tenant shall fail to complete the approved Surrender Plan, or if such Surrender Plan, whether or not approved by Landlord, shall fail to adequately address any residual effect of Tenant HazMat Operations in, on or about the Premises, such failure shall be deemed a failure to vacate in accordance with this Lease, and Landlord shall retain all remedies available under this Lease, at law or equity including, without limitation, the right to collect rent on a holdover basis, and Landlord shall have the right to take such actions as Landlord may deem reasonable or appropriate to assure that the Premises and the Project are surrendered free from any residual impact from Tenant HazMat Operations, the cost of which actions shall be reimbursed by Tenant as Additional Rent, without regard to the limitation set forth in the first paragraph of this Section 28.

(c) Prior to the expiration of the Term, Tenant shall immediately return to Landlord all keys and/or access cards to parking facilities, the Project, restrooms or all or any portion of the Premises furnished to or otherwise procured by Tenant. If any such access card or key is lost, Tenant shall pay to Landlord, at Landlord’s election, either the cost of replacing such lost access card or key or the cost of reprogramming the access security system in which such access card was used or changing the lock or locks opened by such lost key. Any Tenant’s Property, Alterations and property not so removed by Tenant as permitted or required herein shall be deemed abandoned and may be stored, removed, and disposed of by Landlord at Tenant’s expense, and Tenant waives

all claims against Landlord for any damages resulting from Landlord's retention and/or disposition of such property. All obligations of Tenant hereunder not fully performed as of the termination of the Term, including the obligations of Tenant under Section 30 hereof, shall survive the expiration or earlier termination of the Term, including, without limitation, indemnity obligations, payment obligations with respect to Rent and obligations concerning the condition and repair of the Premises.

**29. Waiver of Jury Trial; Consent to Jurisdiction; Prohibited Parties.**

(a) TENANT AND LANDLORD WAIVE ANY RIGHT TO TRIAL BY JURY OR TO HAVE A JURY PARTICIPATE IN RESOLVING ANY DISPUTE, WHETHER SOUNDING IN CONTRACT, TORT, OR OTHERWISE, BETWEEN LANDLORD AND TENANT ARISING OUT OF THIS LEASE OR ANY OTHER INSTRUMENT, DOCUMENT, OR AGREEMENT EXECUTED OR DELIVERED IN CONNECTION HEREWITH OR THE TRANSACTIONS RELATED HERETO.

(b) Landlord and Tenant each hereby (i) irrevocably and unconditionally consents and submits to the jurisdiction of any Federal, state, county or municipal court sitting in the County and State of New York in respect to any action or proceeding concerning any matters arising out of or in any way relating to this Lease; (ii) irrevocably waives all objections as to venue and any and all rights it may have to seek a change of venue with respect to any such action or proceedings if the same is brought in the County of New York; (iii) agrees that this Lease and the rights and obligations of the parties shall be governed by and construed, and all actions, proceedings and all controversies and disputes arising under or of or relating to this Lease shall be resolved in accordance with the internal substantive laws of the State of New York applicable to agreements made and to be wholly performed within the State of New York, (iv) waives any defense to any action or proceeding granted by the laws of any other country or jurisdiction unless such defense is also allowed by the laws of the State of New York and (v) agrees that any final judgment rendered against it in any such action or proceeding shall be conclusive and may be enforced in any other jurisdiction by suit on the judgment or in any other manner provided by law. Tenant hereby represents that it is subject to service of process in the State of New York and covenants that it will remain so subject for the term of this Lease. If for any reason Tenant should cease to be so subject to service of process in the State of New York, Tenant hereby designates and appoints Richard Giroux, Chief Operating Officer, MeiraGTx LLC, 450 East 29<sup>th</sup> Street, New York, NY 10016 as its agent upon whom may be served all process, pleadings, notices or other papers which may be served upon Tenant as a result of any of its obligations under this Lease, and if such agent shall cease to act or otherwise cease to be subject to service of process in the State of New York, Tenant designates and appoints the Secretary of State of New York as its agent for service; provided, however, that the serving of such process, pleadings, notices or other papers shall not constitute a condition to Tenant's obligations hereunder. For the term of this Lease, Tenant's agent designated herein shall accept and acknowledge in Tenant's behalf service of any and all process in any such suit, action or proceeding brought in any such court. Tenant agrees and consents that any such service of process upon such agents and written notice of such service to the Lessee in the manner set forth herein shall be taken and held to be valid personal service upon Tenant whether or not Tenant shall then be doing, or at any time shall have done, business within the State of New York and that any such service of process shall be of the same force and validity as if service were made upon Tenant according to the laws governing the validity and requirements of



such service in the State of New York, and waive all claim of error by reason of any such service. Such agents shall not have any power or authority to enter into any appearance or to file any pleadings in connection with any suit, action or other legal proceedings against Tenant or to conduct the defense of any such suit, action or any other legal proceeding except as expressly authorized by Tenant.

(c) Tenant represents and warrants to Landlord that (i) it and each Affiliate or Principal directly or indirectly owning an interest in it is not a Prohibited Entity (as defined in Section 29(d)), (ii) none of the funds or other assets of it constitute property of, or are beneficially owned, directly or indirectly, by, any Person (as defined in Section 29(d)) on the List (as defined in Section 29(d)), (iii) no Person on the List has any interest of any nature whatsoever in it (whether directly or indirectly), and (iv) none of its funds have been derived from any unlawful activity with the result that the investment in it is prohibited by law or that this Lease is in violation of law. Tenant covenants and agrees (I) to comply with all Legal Requirements relating to money laundering, anti-terrorism, trade embargos and economic sanctions, now or hereafter in effect, (II) to immediately notify the other in writing if any of the representations, warranties or covenants set forth in this Section 29(c) are no longer true or have been breached or if it has a reasonable basis to believe that they may no longer be true or have been breached, (III) not to use funds from any Person on the List to make any payment due to Landlord under this Lease and (IV) at the request of the other, to provide such information as may be reasonably requested by Landlord to determine the other's compliance with the terms hereof. Tenant hereby acknowledges and agrees that inclusion on the List of Tenant or any Affiliate or Principal of Tenant at any time during this Lease Term shall be a material default of this Lease. Tenant, and all beneficial owners of Tenant, are currently (i) in compliance with and shall at all times during the Term of this Lease remain in compliance with the regulations of the Office of Foreign Assets Control ("**OFAC**") of the U.S. Department of Treasury and any statute, executive order, or regulation relating thereto (collectively, the "**OFAC Rules**"), (ii) not listed on, and shall not during the Term of this Lease be listed on, the Specially Designated Nationals and Blocked Persons List, Foreign Sanctions Evaders List, or the Sectoral Sanctions Identifications List, which are all maintained by OFAC and/or on any other similar list maintained by OFAC or other governmental authority pursuant to any authorizing statute, executive order, or regulation, and (iii) not a person or entity with whom a U.S. person is prohibited from conducting business under the OFAC Rules. Notwithstanding anything to the contrary contained herein, Tenant shall not permit the Premises or any portion thereof to be used or occupied by any Person on the List (on a permanent, temporary or transient basis), and any such use or occupancy of the Premises by any such Person shall be a material default of this Lease. Notwithstanding anything to the contrary contained in this Section 29(c), so long as Landlord or its ultimate parent is a company whose capital stock is traded on a recognized public exchange, Landlord makes no representations or warranties as to the persons or entities owning an interest in Landlord.

(d) The following capitalized terms, whenever used in this Lease, shall have the respective meanings ascribed to such terms as follows: (i) "**Prohibited Entity**" shall mean (A) any Prohibited Person or (B) any Person that is identified on the List; (ii) "**Prohibited Person**" shall mean (A) any Person (1) that is in default, after notice and beyond the expiration of any applicable cure period, of such Person's obligations under any material written agreement with the City, the State of New York or any of their instrumentalities, or (2) that directly controls, is controlled by, or is under common control with a Person that is in default, after notice and beyond

the expiration of any applicable cure period, of such Person's obligations under any material written agreement with the City, the State of New York or any of their instrumentalities, unless, in each instance, such default or breach either (a) has been waived in writing by the City, the State of New York or any of their instrumentalities as the case may be, or (b) is being disputed in a court of law, administrative proceeding, arbitration or other forum, or (c) is cured within 30 days after a determination and notice to Tenant from Landlord that such Person is a Prohibited Person as a result of such default; (B) any Person that is an Organized Crime Figure; (C) any government, or any Person that is directly or indirectly controlled (rather than only regulated) by a government, that is finally determined to be in violation of (including, but not limited to, any participant in an international boycott in violation of) the Export Administration Act of 1979, as amended, or any successor statute, or the regulations issued pursuant thereto, or any government that is, or any Person that, directly or indirectly, is controlled (rather than only regulated) by a government that is subject to the regulations or controls thereof; (D) any government, or any Person that, directly or indirectly, is controlled (rather than only regulated) by a government, the effects or the activities of which are regulated or controlled pursuant to regulations of the United States Treasury Department or executive orders of the President of the United States of America issued pursuant to the Trading with the Enemy Act of 1917, as amended; (E) any Person that is in default in the payment to the City of any real estate taxes, sewer rents or water charges totaling more than \$10,000, unless such default is then being contested in good faith in accordance with applicable Legal Requirements or unless such default is cured within 30 days after a determination and notice to Tenant from Landlord that such Person is a Prohibited Person as a result of such default; or (F) any Person (1) that has solely owned, at any time during the 3-year period immediately preceding a determination of whether such Person is a Prohibited Person, any property which, while in the ownership of such Person, was acquired by the City by in rem tax foreclosure, other than a property in which the City has released or is in the process of releasing its interest pursuant to the Administrative Code of the City, or (2) that, directly or indirectly controls, is controlled by, or is under common control with a Person that has owned, at any time in the 3-year period immediately preceding a determination of whether such Person is a Prohibited Person, any property which, while in the ownership of such Person, was acquired by the City by in rem tax foreclosure, other than a property in which the City has released or is in the process of releasing its interest to such Person pursuant to the Administrative Code of the City; (iii) "**Organized Crime Figure**" shall mean any Person (A) who has been convicted in a criminal proceeding for a felony or any crime involving moral turpitude or that is an organized crime figure or is reputed to have substantial business or other affiliations with an organized crime figure, or (B) who, directly or indirectly controls, is controlled by, or is under common control with, a Person who has been convicted in a criminal proceeding for a felony or any crime involving moral turpitude or that is an organized crime figure or is reputed to have substantial business or other affiliations with an organized crime figure; and, the determination as to whether any Person is an organized crime figure or is reputed to have substantial business or other affiliations with an organized crime figure shall be within the sole discretion of Landlord, which discretion shall be exercised in good faith, or as determined by the Ground Landlord in accordance with the terms of the Ground Lease; (iv) "**Person**" shall mean (A) an individual, corporation, limited liability company, partnership, joint venture, estate, trust, unincorporated association or other business entity, (B) any federal, state, county or municipal government (or any bureau, department, agency or instrumentality thereof), and (C) any fiduciary acting in such capacity on behalf of any of the foregoing; (v) "**List**" shall mean, collectively, as updated from time to time, the Specially Designated Nationals and Blocked Persons List, Foreign

Sanctions Evaders List, or the Sectoral Sanctions Identifications List, which are all maintained by OFAC and/or on any other similar list maintained by OFAC pursuant to any authorizing statute, executive order or regulation; and (vi) “**Principal**” shall mean, in respect of Tenant, any Person that is a direct or indirect owner of an equity interest in Tenant.

### 30. **Environmental Requirements.**

(a) **Prohibition/Compliance/Indemnity.** Tenant shall not cause or permit any Hazardous Materials (as hereinafter defined) to be brought upon, kept, used, stored, handled, treated, generated in or about, or released or disposed of from, the Premises or the Project in violation of applicable Environmental Requirements (as hereinafter defined) by Tenant or any Tenant Party. If Tenant breaches the obligation stated in the preceding sentence, or if the presence of Hazardous Materials in the Premises during the Term or any holding over results in contamination of the Premises, the Project or any adjacent property, or if contamination of the Premises, the Project or any adjacent property by Hazardous Materials brought into, kept, used, stored, handled, treated, generated in or about, or released or disposed of from, the Premises by anyone other than Landlord and Landlord’s employees, agents and contractors otherwise occurs during the Term or any holding over, Tenant hereby indemnifies and shall defend and hold Landlord, its officers, directors, employees, agents and contractors harmless from any and all actions (including, without limitation, remedial or enforcement actions of any kind, administrative or judicial proceedings, and orders or judgments arising out of or resulting therefrom), costs, claims, damages (including, without limitation, punitive damages and damages based upon diminution in value of the Premises or the Project, or the loss of, or restriction on, use of the Premises or any portion of the Project), expenses (including, without limitation, attorneys’, consultants’ and experts’ fees, court costs and amounts paid in settlement of any claims or actions), fines, forfeitures or other civil, administrative or criminal penalties, injunctive or other relief (whether or not based upon personal injury, property damage, or contamination of, or adverse effects upon, the environment, water tables or natural resources), liabilities or losses (collectively, “**Environmental Claims**”) which arise during or after the Term as a result of such contamination. This indemnification of Landlord by Tenant includes, without limitation, costs incurred in connection with any investigation of site conditions or any cleanup, treatment, remedial, removal, or restoration work required by any federal, state or local Governmental Authority because of Hazardous Materials present in the air, soil or ground water above, on, or under the Premises. Without limiting the foregoing, if the presence of any Hazardous Materials on the Premises, the Building, the Project or any adjacent property caused or permitted by Tenant or any Tenant Party results in any contamination of the Premises, the Building, the Project or any adjacent property, Tenant shall promptly take all actions at its sole expense and in accordance with applicable Environmental Requirements as are necessary to return the Premises, the Building, the Project or any adjacent property to the condition existing prior to the time of such contamination, provided that Landlord’s approval of such action shall first be obtained, which approval shall not unreasonably be withheld so long as such actions would not potentially have any material adverse long-term or short-term effect on the Premises, the Building or the Project.

(b) **Business.** Landlord acknowledges that it is not the intent of this Section 30 to prohibit Tenant from using the Premises for the Permitted Use. Tenant may operate its business according to prudent industry practices so long as the use or presence of Hazardous Materials is strictly and properly monitored according to all then applicable Environmental Requirements. As

a material inducement to Landlord to allow Tenant to use Hazardous Materials in connection with its business, Tenant agrees to deliver to Landlord prior to the Commencement Date a list identifying each type of Hazardous Materials to be brought upon, kept, used, stored, handled, treated, generated on, or released or disposed of from, the Premises and setting forth any and all governmental approvals or permits required in connection with the presence, use, storage, handling, treatment, generation, release or disposal of such Hazardous Materials on or from the Premises (“**Hazardous Materials List**”). Tenant shall deliver to Landlord an updated Hazardous Materials List at least once a year and shall also deliver an updated list before any new Hazardous Material is brought onto, kept, used, stored, handled, treated, generated on, or released or disposed of from, the Premises. Tenant shall deliver to Landlord true and correct copies of the following documents (the “**Haz Mat Documents**”) relating to the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials prior to the Commencement Date, or if unavailable at that time, concurrent with the receipt from or submission to a Governmental Authority: permits; approvals; reports and correspondence; storage and management plans, notice of violations of any Legal Requirements; plans relating to the installation of any storage tanks to be installed in or under the Project (provided, said installation of tanks shall only be permitted after Landlord has given Tenant its written consent to do so, which consent may be withheld in Landlord’s sole and absolute discretion); all closure plans or any other documents required by any and all federal, state and local Governmental Authorities for any storage tanks installed in, on or under the Project for the closure of any such tanks; and a Surrender Plan (to the extent surrender in accordance with Section 28 cannot be accomplished in 3 months). Tenant is not required, however, to provide Landlord with any portion(s) of the Haz Mat Documents containing information of a proprietary nature which, in and of themselves, do not contain a reference to any Hazardous Materials or hazardous activities. It is not the intent of this Section 30(b) to provide Landlord with information which could be detrimental to Tenant’s business should such information become possessed by Tenant’s competitors.

(c) **Tenant Representation and Warranty.** Tenant hereby represents and warrants to Landlord that (i) neither Tenant nor any of its legal predecessors has been required by any prior landlord, lender or Governmental Authority at any time to take remedial action in connection with Hazardous Materials contaminating a property which contamination was permitted by Tenant of such predecessor or resulted from Tenant’s or such predecessor’s action or use of the property in question, and (ii) Tenant is not subject to any enforcement order issued by any Governmental Authority in connection with the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials (including, without limitation, any order related to the failure to make a required reporting to any Governmental Authority). If Landlord determines that this representation and warranty was not true as of the date of this lease, Landlord shall have the right to terminate this Lease in Landlord’s sole and absolute discretion.

(d) **Testing.** Landlord shall have the right to conduct annual tests of the Premises to determine whether any contamination of the Premises or the Project has occurred as a result of Tenant’s use. Tenant shall be required to pay the cost of such annual test of the Premises; provided, however, that if Tenant conducts its own tests of the Premises using third party contractors and test procedures acceptable to Landlord which tests are certified to Landlord, Landlord shall accept such tests in lieu of the annual tests to be paid for by Tenant. In addition, at any time, and from time to time, prior to the expiration or earlier termination of the Term, Landlord shall have the right to conduct appropriate tests of the Premises and the Project to determine if contamination has

occurred as a result of Tenant's use of the Premises. In connection with such testing, upon the request of Landlord, Tenant shall deliver to Landlord or its consultant such non-proprietary information concerning the use of Hazardous Materials in or about the Premises by Tenant or any Tenant Party. If contamination has occurred for which Tenant is liable under this Section 30, Tenant shall pay all costs to conduct such tests. If no such contamination is found, Landlord shall pay the costs of such tests (which shall not constitute an Operating Expense).

Landlord shall provide Tenant with a copy of all third party, non-confidential reports and tests of the Premises made by or on behalf of Landlord during the Term without representation or warranty and subject to a confidentiality agreement. Tenant shall, at its sole cost and expense, promptly and satisfactorily remediate any environmental conditions identified by such testing in accordance with all Environmental Requirements. Landlord's receipt of or satisfaction with any environmental assessment in no way waives any rights which Landlord may have against Tenant.

(e) **Underground Tanks.** If underground or other storage tanks storing Hazardous Materials located on the Premises or the Project are used by Tenant or are hereafter placed on the Premises or the Project by Tenant, Tenant shall install, use, monitor, operate, maintain, upgrade and manage such storage tanks, maintain appropriate records, obtain and maintain appropriate insurance, implement reporting procedures, properly close any underground storage tanks, and take or cause to be taken all other actions necessary or required under applicable state and federal Legal Requirements, as now exist or may hereafter be adopted or amended in connection with the installation, use, maintenance, management, operation, upgrading and closure of such storage tanks.

(f) **Tenant's Obligations.** Tenant's obligations under this Section 30 shall survive the expiration or earlier termination of this Lease. During any period of time after the expiration or earlier termination of this Lease required by Tenant or Landlord to complete the removal from the Premises of any Hazardous Materials (including, without limitation, the release and termination of any licenses or permits restricting the use of the Premises and the completion of the approved Surrender Plan), Tenant shall continue to pay the full Rent in accordance with this Lease attributable to any portion of the Premises not relet by Landlord in Landlord's sole discretion, which Rent shall be prorated daily.

(g) **Definitions.** As used herein, the term "**Environmental Requirements**" means all applicable present and future statutes, regulations, ordinances, rules, codes, judgments, orders or other similar enactments of any Governmental Authority regulating or relating to health, safety, or environmental conditions on, under, or about the Premises or the Project, or the environment, including without limitation, the following: the Comprehensive Environmental Response, Compensation and Liability Act; the Resource Conservation and Recovery Act; and all state and local counterparts thereto, and any regulations or policies promulgated or issued thereunder. As used herein, the term "**Hazardous Materials**" means and includes any substance, material, waste, pollutant, or contaminant listed or defined as hazardous or toxic, or regulated by reason of its impact or potential impact on humans, animals and/or the environment under any Environmental Requirements, asbestos and petroleum, including crude oil or any fraction thereof, natural gas liquids, liquefied natural gas, or synthetic gas usable for fuel (or mixtures of natural gas and such synthetic gas). As defined in Environmental Requirements, Tenant is and shall be deemed to be the "**operator**" of Tenant's "**facility**" and the "**owner**" of all Hazardous Materials brought on the Premises by Tenant or any Tenant Party, and the wastes, by-products, or residues generated, resulting, or produced therefrom.

(h) Tenant shall comply with (or cause to be complied with) all applicable federal, state and local laws concerning any Regulated Medical Waste that Tenant or any subtenant or occupant of the Premises produces, brings on, keeps, uses, stores, disposes or treats in or about the Premises or transported from the Premises. Tenant shall also comply with all applicable federal, state and local laws related to the health and safety of its employees. **“Regulated Medical Waste”** means any substance, gas, material or chemical, or any part thereof, which is defined as or included in the definition of “regulated medical waste” or words of similar import under any Requirement, including by not limited to Section 27-1502 of the New York Environmental Conservation Law, 42 U.S.C. Section 6901 et seq., the Medical Waste Tracking Act of 1988 and Track XIII of the New York State Public Health Law and the regulations promulgated thereunder.

31. **Tenant’s Remedies/Limitation of Liability.** Landlord shall not be in default hereunder unless Landlord fails to perform any of its obligations hereunder within 30 days after written notice from Tenant specifying such failure (unless such performance will, due to the nature of the obligation, require a period of time in excess of 30 days, then after such period of time as is reasonably necessary). Upon any default by Landlord, Tenant shall give notice by registered or certified mail to any Holder of a Mortgage covering the Premises and to any landlord of any lease of property in or on which the Premises are located and Tenant shall offer such Holder and/or landlord a reasonable opportunity to cure the default, including time to obtain possession of the Project by power of sale or a judicial action if the same should prove necessary to effect a cure; provided Landlord shall have furnished to Tenant in writing the names and addresses of all such persons who are to receive such notices. All obligations of Landlord hereunder shall be construed as covenants, not conditions; and, except as may be otherwise expressly provided in this Lease, Tenant may not terminate this Lease for breach of Landlord’s obligations hereunder.

All obligations of Landlord under this Lease will be binding upon Landlord only during the period of its ownership of the Premises and not thereafter. The term **“Landlord”** in this Lease shall mean only the owner for the time being of the Premises. Upon the transfer by such owner of its interest in the Premises, such owner shall thereupon be released and discharged from all obligations of Landlord thereafter accruing, but such obligations shall be binding during the Term upon each new owner for the duration of such owner’s ownership.

32. **Inspection and Access.** Landlord and its agents, representatives, and contractors may enter the Premises at any reasonable time to inspect the Premises and to make such repairs as may be required or permitted pursuant to this Lease and for any other business purpose. Landlord and Landlord’s representatives may enter the Premises during business hours on not less than 48 hours’ advance written notice (except in the case of emergencies in which case no such notice shall be required and such entry may be at any time) for the purpose of effecting any such repairs, inspecting the Premises, showing the Premises to prospective purchasers and, during the last year of the Term, to prospective tenants or for any other business purpose. Landlord may erect a suitable sign on the Premises stating the Premises are available to let or that the Project is available for sale. Landlord may grant easements, make public dedications, designate Common Areas and create restrictions on or about the Premises, provided that no such easement, dedication, designation or restriction materially, adversely affects Tenant’s use or occupancy of the Premises for the

Permitted Use. At Landlord's request, Tenant shall execute such instruments as may be necessary for such easements, dedications or restrictions. Tenant shall at all times, except in the case of emergencies, have the right to escort Landlord or its agents, representatives, contractors or guests while the same are in the Premises, provided such escort does not materially and adversely affect Landlord's access rights hereunder.

33. **Security.** Tenant acknowledges and agrees that security devices and services, if any, while intended to deter crime may not in given instances prevent theft or other criminal acts and that Landlord is not providing any security services with respect to the Premises. Tenant agrees that Landlord shall not be liable for, and Tenant waives any claim against Landlord with respect to, any loss by theft or any other damage suffered or incurred by Tenant in connection with any unauthorized entry into the Premises or any other breach of security with respect to the Premises. Tenant shall be solely responsible for the personal safety of Tenant's officers, employees, agents, contractors, guests and invitees while any such person is in, on or about the Premises, the Building and/or the Project. Tenant shall at Tenant's cost obtain insurance coverage to the extent Tenant desires protection against such criminal acts. All employees, contractors and/or agents of any provider of security services to the Premises engaged by Tenant shall be prohibited from carrying firearms (e.g. handguns, rifles, shotguns, etc.). Each individual employee or independent contractor of any such service provider shall have been registered with Landlord by facsimile or mail at least 48 hours in advance of such person arriving at the Project to perform service, which registration shall require such personal information and history, and photographs, as Landlord shall reasonably require.

34. **Force Majeure.** Landlord shall not be responsible or liable for delays in the performance of its obligations hereunder when caused by, related to, or arising out of acts of God, strikes, lockouts, or other labor disputes, vandalism, embargoes, quarantines, weather, national, regional, or local disasters, calamities, or catastrophes, inability to obtain labor or materials (or reasonable substitutes therefor) at reasonable costs or failure of, or inability to obtain, utilities necessary for performance, governmental restrictions, orders, limitations, regulations, or controls, national emergencies, delay in issuance or revocation of permits, enemy or hostile governmental action, terrorism, insurrection, riots, civil disturbance or commotion, fire or other casualty, and other causes or events beyond the reasonable control of Landlord ("**Force Majeure**").

35. **Brokers, Entire Agreement, Amendment.** Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, "**Broker**") in connection with this transaction and that no Broker brought about this transaction other than Cushman & Wakefield, Inc. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than the broker, if any named in this Section 35, claiming a commission or other form of compensation by virtue of having dealt with Tenant or Landlord, as applicable, with regard to this leasing transaction.

36. **Limitation on Landlord's Liability.** NOTWITHSTANDING ANYTHING SET FORTH HEREIN OR IN ANY OTHER AGREEMENT BETWEEN LANDLORD AND TENANT TO THE CONTRARY: (A) LANDLORD AND THE CONDOMINIUM BOARD SHALL NOT BE LIABLE TO TENANT OR ANY OTHER PERSON FOR (AND TENANT AND EACH SUCH OTHER PERSON ASSUME ALL RISK OF) LOSS, DAMAGE OR INJURY, WHETHER ACTUAL OR CONSEQUENTIAL TO: TENANT'S PERSONAL

PROPERTY OF EVERY KIND AND DESCRIPTION, INCLUDING, WITHOUT LIMITATION TRADE FIXTURES, EQUIPMENT, INVENTORY, SCIENTIFIC RESEARCH, SCIENTIFIC EXPERIMENTS, LABORATORY ANIMALS, PRODUCT, SPECIMENS, SAMPLES, AND/OR SCIENTIFIC, BUSINESS, ACCOUNTING AND OTHER RECORDS OF EVERY KIND AND DESCRIPTION KEPT AT THE PREMISES AND ANY AND ALL INCOME DERIVED OR DERIVABLE THEREFROM; (B) THERE SHALL BE NO PERSONAL RECOURSE TO LANDLORD OR THE CONDOMINIUM BOARD FOR ANY ACT OR OCCURRENCE IN, ON OR ABOUT THE PREMISES OR ARISING IN ANY WAY UNDER THIS LEASE OR ANY OTHER AGREEMENT BETWEEN LANDLORD AND TENANT WITH RESPECT TO THE SUBJECT MATTER HEREOF AND ANY LIABILITY OF LANDLORD HEREUNDER SHALL BE STRICTLY LIMITED SOLELY TO LANDLORD'S INTEREST IN THE PROJECT OR ANY PROCEEDS FROM SALE OR CONDEMNATION THEREOF AND ANY INSURANCE PROCEEDS PAYABLE IN RESPECT OF LANDLORD'S INTEREST IN THE PROJECT OR IN CONNECTION WITH ANY SUCH LOSS; AND (C) IN NO EVENT SHALL ANY PERSONAL LIABILITY BE ASSERTED AGAINST ANY OF LANDLORD'S OR THE CONDOMINIUM BOARD'S OFFICERS, DIRECTORS, EMPLOYEES, AGENTS OR CONTRACTORS. UNDER NO CIRCUMSTANCES SHALL LANDLORD OR ANY OF LANDLORD'S OR THE CONDOMINIUM'S BOARD'S OFFICERS, DIRECTORS, EMPLOYEES, AGENTS OR CONTRACTORS BE LIABLE FOR INJURY TO TENANT'S BUSINESS OR FOR ANY LOSS OF INCOME OR PROFIT THEREFROM.

37. **Severability.** If any clause or provision of this Lease is illegal, invalid or unenforceable under present or future laws, then and in that event, it is the intention of the parties hereto that the remainder of this Lease shall not be affected thereby. It is also the intention of the parties to this Lease that in lieu of each clause or provision of this Lease that is illegal, invalid or unenforceable, there be added, as a part of this Lease, a clause or provision as similar in effect to such illegal, invalid or unenforceable clause or provision as shall be legal, valid and enforceable.

38. **Signs; Exterior Appearance.** Tenant shall not, without the prior written consent of Landlord, which may be granted or withheld in Landlord's sole discretion: (i) attach any awnings, exterior lights, decorations, balloons, flags, pennants, banners, painting or other projection to any outside wall of the Project, (ii) use any curtains, blinds, shades or screens other than Landlord's standard window coverings, (iii) coat or otherwise sunscreen the interior or exterior of any windows, (iv) place any bottles, parcels, or other articles on the window sills, (v) place any equipment, furniture or other items of personal property on any exterior balcony, or (vi) paint, affix or exhibit on any part of the Premises or the Project any signs, notices, window or door lettering, placards, decorations, or advertising media of any type which can be viewed from the exterior of the Premises. Interior signs on doors and the directory tablet shall be inscribed, painted or affixed for Tenant by Landlord at the sole cost and expense of Tenant, and shall be of a size, color and type acceptable to Landlord. Nothing may be placed on the exterior of corridor walls or corridor doors other than Landlord's standard lettering. The directory tablet shall be provided exclusively for the display of the name and location of tenants of the Project.

39. **Zoning Rights.** At all times, Landlord shall have the right, and Tenant shall not have the right, (i) to cause all or any part of the Premises and/or the zoning lot upon which the Building is located in whole or in part (hereinafter referred to solely for purposes of this Section 39



as the “**Land**”) and/or the Building, to be combined with any other land, condominium units or other premises so as to constitute the combined premises into a single zoning “lot” or “development” or “enlargement” as those terms are now, or may hereafter be, defined in the Zoning Resolution of The City of New York (the “**Zoning Resolution**”), (ii) to cause any lot, development or enlargement at any time constituting or including all or any part of the Premises, the Land or the Building to be subdivided into two or more lots, developments or enlargements, (iii) to cause development rights (whether from the Land or other premises) to be transferred to any such lot, development or enlargement, (iv) to cause other combinations, subdivisions and transfers to be effected, whether similar or dissimilar to those now permitted by law or (v) to exploit, sell, convey, lease or otherwise transfer any so called “air rights,” “air space,” “zoning rights” or “development rights” above or appurtenant to the Land and/or the Building provided that and for so long as the foregoing actions described in clauses (i) through (v) do not (a) adversely affect Tenant or Tenant’s use and enjoyment of the Premises, (b) increase the Base Rent or any Additional Rent, (c) otherwise increase the obligations of Tenant or the rights of Landlord under this Lease or (d) otherwise decrease the obligations of Landlord or the rights of Tenant under this Lease. Tenant hereby acknowledges that it is not a “party in interest” as defined in the Zoning Resolution, and shall not and cannot become a “party in interest” under any circumstances by virtue of its leasehold interest hereunder. Tenant further acknowledges that neither Tenant nor the estate or interest of Tenant hereunder would be “adversely affected” (within the meaning of the Zoning Resolution) by any development of the Land or the Building or any such combined premises nor by the filing of any declaration combining all or a part of the Land and/or the Building with any other premises and that Tenant’s estate and interest hereunder are not and would not be superior to any such declaration. Notwithstanding the foregoing, in the event that Tenant is deemed to have any of the rights disclaimed above, or is deemed to be a party in interest, Tenant hereby transfers such rights and any rights as a party in interest to Landlord. In furtherance thereof, Tenant will within 3 business days after written request by Landlord execute and deliver to Landlord a waiver of its right to join in a Declaration of Restrictions pursuant to Section 12-10 of the Zoning Resolution.

40. **Excavation.** In the event that an excavation, or any construction, should be undertaken in connection with the Building or other purposes upon land adjacent to the Building and/or the Project, or should be authorized to be made, Tenant shall, upon reasonable prior notice, if necessary, afford to the person or persons causing or authorized to cause such excavation or construction or other purpose, the right, for brief periods of time and in a manner so as to avoid any material interference with Tenant’s business, subject to such reasonable conditions as Tenant may reasonably impose, to enter upon the Premises for the purpose of doing such work as shall reasonably be necessary to protect or preserve the wall or walls of the Building, from injury or damage and to support them by proper foundations, pinning and/or underpinning, or otherwise.

41. **Employment Reporting and Requirements.**

(a) With regard to each annual period from July 1 through June 30 from and after the date of this Lease if requested by Landlord, Tenant shall complete with regard to itself and any of its subtenants, items 1-5, 15 and 16 of the Employment and Benefits Report (with the dates therein updated to reflect the applicable Fiscal Year) attached as **Exhibit P** to the Ground Lease, and Tenant shall sign such report and submit it to Landlord before July 15 immediately following such annual period; and

(b) Tenant shall, in good faith, consider such proposals as the City and/or City-related entities may make with regard to any jobs Tenant may seek to fill in relation to its activities on or concerning the Premises, and shall provide the City and such entities with the opportunity to (A) refer candidates who are City residents having the requisite experience for the positions in question, and/or (B) create a program to train City residents for those jobs, and to report to Ground Landlord, upon Ground Landlord's request, regarding the status of its consideration of such proposals (it being understood that Tenant shall not be required to hire any candidate which Tenant, in good faith, considers unqualified for the applicable position).

(c) Both Landlord and Ground Landlord and their respective designees shall be beneficiaries of each such agreement by Tenant. Landlord hereby reserves the right, on behalf of itself and Ground Landlord, and their respective designees, as such third party beneficiaries, to seek specific performance by Tenant, at the expense of Tenant, of the aforesaid obligations contained in this Section 41.

42. **Prohibited Distinctions.** Tenant covenants and agrees to be bound by the following covenants, which shall be binding for the benefit of Landlord and Ground Landlord and enforceable by Landlord and Ground Landlord against Tenant to the fullest extent permitted by law and equity:

(a) Tenant (and any lessees of the Premises or any part thereof) shall comply with all applicable federal, state, and local laws in effect from time to time prohibiting discrimination or segregation by reason of age, race, creed, religion, sex, color, national origin, ancestry, sexual orientation or affectional preference, disability, or marital status (collectively, "**Prohibited Distinctions**") in the lease or occupancy of the Premises.

(b) Tenant shall not effect or execute any agreement, lease, conveyance, or other instrument whereby the lease or occupancy of the Premises, or any part thereof, is restricted upon the basis of any Prohibited Distinction.

(c) Tenant (and any lessees of the Premises or any part thereof) shall include the covenants of (a) and (b) in any agreement, sublease, conveyance, or other instrument with respect to the lease or occupancy of the Premises.

43. **IDA Lease Requirements.** Tenant shall provide, and shall cause any subtenant or other occupant of the Premises to provide, to Landlord and to any other entity specified by Landlord in writing, the information that Landlord needs in order to satisfy the reporting requirements set forth in the provisions of the IDA Lease excerpted on **Exhibit M** hereto, as the same may be modified from time to time by the governmental entities requiring the same. Tenant represents, and shall cause and subtenant or other occupant of the Premises to represent with respect to itself (in place of "Tenant"), that either: (A) Tenant's occupancy at the Project will not result in the removal of a plant or facility of Tenant located outside of the City, but within the State of New York, to the Project or in the abandonment of one or more of such plants or facilities of such Tenant located outside of the City but within the State of New York or (B) Tenant's location at the Project is reasonably necessary to discourage Tenant from removing its business to a location outside of the State of New York or is reasonably necessary to preserve Tenant's competitive position in its industry.

44. **ICIP.** Landlord hereby notifies Tenant that Landlord intends to avail itself of the Industrial and Commercial Incentive Program (“**ICIP**”). In connection therewith, all of Tenant’s construction managers, contractors and subcontractors employed in connection with construction work at the Building shall be contractually required by Tenant to comply with the New York City Department of Small Business Services/Division of Labor Services (“**DLS**”) requirements applicable to construction projects benefiting from the ICIP. Such compliance, as of the date hereof, includes the following: the submission and approval of a Construction Employment Report, attendance at a pre-construction conference with representatives of the DLS and adherence to the provisions of Article 22 of the ICIP Rules and Regulations, the provisions of New York City Charter Chapter 13-B and the provisions of Executive Order No. 50 (1980). Furthermore, at Landlord’s request, Tenant shall (A) report to Landlord the number of workers permanently engaged in employment in the Premises, the nature of each worker’s employment and, to the extent applicable, the New York City residency of each worker, (B) provide access to the Premises by employees and agents of the Department (as such term is defined in the ICIP Rules and Regulations) at all reasonable times upon reasonable advance notice, and (C) enforce the contractual obligations of Tenant’s construction managers, contractors and subcontractors to comply with the DLS requirements.

45. **Release of Portion(s) of the Project.** Landlord, at any time and from time to time, shall have the right to subdivide, transfer title to, or enter into a ground lease or long-term net lease (a “**Partial Conveyance**”) of, or convert to a condominium form of ownership, any portion of the Project (including, for example, by transferring one or more of the Project’s buildings and/or another portion or portions of the Project) to another Person not in Control of, Controlled by or under common Control with, Landlord, which such Partial Conveyance may reduce the size of the Project. In the event of such a Partial Conveyance by Landlord, Landlord and Tenant agree to enter into an amendment of this Lease in form reasonably satisfactory to Landlord and Tenant to adjust the definitions of Real Property and Project, if necessary and in accordance with the conditions set forth in this Section 45, to describe accurately the land and improvements constituting the remaining portion of the Land and Project after such Partial Conveyance; to increase Tenant’s Share, if necessary to reflect the transfer of the portion of the Land and/or the Project included in such Partial Conveyance; and to make any other changes that may be necessary or appropriate so that Tenant continues to be responsible for its other obligations, including the payment of Rent, under this Lease and to enjoy its rights and privileges under this Lease, subject to and in accordance with this Section 45.

46. **Shared Lab Area.**

(a) **General Provisions.** Notwithstanding anything to the contrary herein, Tenant shall have a license, on a non-exclusive basis in common with other tenants and users of the tenth (10th) floor of the Building, to use the Shared Lab Area for the Permitted Use, in accordance with the Rules and Regulations applicable thereto and all Legal Requirements, but such access and use shall be subject to the terms of the Superior Instruments (as defined in Section 27). The Shared Lab Area contains certain equipment, furnishings, systems, and personal property, as more particularly described on **Exhibit I** (collectively, the “**Shared Lab Systems**”). The license granted hereby is personal to Tenant and shall not, except as provided in the next sentence, be assigned or otherwise pledged or transferred, directly or indirectly. In the case of a Permitted Assignment, Tenant shall have no further right to use the Shared Lab Area and the Shared Lab Systems in accordance with

the terms and conditions of this Lease; provided, however, that the following shall have the non-exclusive license to use the Shared Lab Systems in accordance with the terms and conditions of this Lease: (i) a subtenant approved by Landlord in accordance with the provisions of this Lease that subleases 50% or more of the Premises, and (ii) an assignee permitted under a Permitted Assignment.

(b) **Relocation/Modification of Shared Lab Area.** Landlord shall have the right at any time and from time to time in the exercise of its sole and absolute subjective discretion to reconfigure, relocate, or modify the Shared Lab Area and to revise, expand, suspend, terminate, or discontinue any of the Shared Lab Systems. Landlord shall provide reasonable notice to Tenant of the relocation, suspension, termination, or discontinuance of any Shared Lab Systems as long as Landlord has actual knowledge of any such relocation, suspension, termination, or discontinuance.

(c) **Interference.** Tenant shall use the Shared Lab Area and the Shared Lab Systems in a manner that will not interfere with the rights of any tenants or occupants in the Building or users of the Shared Lab Area or the providers of the services associated with the Shared Lab Systems. Landlord assumes no responsibility for enforcing Tenant's rights or for protecting the Shared Lab Area from any person or entity, including, but not limited to, other tenants or occupants of the Building or users of the Shared Lab Area.

(d) **Limitations.** Landlord's sole obligation for providing the Shared Lab Systems shall be: (A) to provide the Shared Lab Systems as is determined by Landlord in the exercise of its sole and absolute subjective discretion, and (B) to contract with one or more third parties to maintain the Shared Lab Systems that are deemed by Landlord in the exercise of its sole and absolute subjective discretion to need periodic maintenance in accordance with the manufacturer's or supplier's standard guidelines or otherwise. During any period of replacement, repair, or maintenance of the Shared Lab Systems when they are not operational (including, but not limited to, any delays thereto due to the inability to obtain parts or replacements), Landlord shall have no obligation to provide Tenant with alternative, supplemental, temporary, or back-up Shared Lab Systems. Tenant acknowledges and agrees that, because the Shared Lab Area and Shared Lab Systems are provided for the benefit of all tenants and users of the tenth (10th) floor of the Building, Landlord may reduce the Shared Lab Area and/or Shared Lab Systems and/or the resources therein from time to time in response to a lack of usage by such tenants or obsolescence or similar reasons and users and may increase, replace or otherwise modify the Shared Lab Area and/or Shared Lab Systems and/or resources therein from time to time in response to the needs of such tenants and users. Landlord shall have no liability for any such reduction, increase, replacement or modification of the Shared Lab Area and/or Shared Lab Systems, and none of the foregoing shall reduce the Base Rent payable by Tenant hereunder. Tenant acknowledges and agrees that increases, replacements and/or modifications of the Shared Lab Area and/or Shared Lab Systems may result in an increase in Operating Expenses (SLA), and Tenant agrees to pay Tenant's Share (SLA) of any such increase in accordance with Section 46(h) below. The terms and provisions of this paragraph shall survive the expiration or earlier termination of this Lease.

(e) **No Warranties.** Landlord makes no warranties of any kind, express or implied, with respect to the Shared Lab Area and Shared Lab Systems, and Landlord disclaims any such warranties. Without limiting the foregoing, Tenant expressly acknowledges and agrees that Landlord does not guaranty or warrant that the Shared Lab Systems will be operational at all times,

will be of sufficient capacity to accommodate Tenant's use thereof, will be free of Hazardous Materials, or will function or perform adequately, and Landlord shall not be liable for any damages resulting from the failure of the Shared Lab Systems.

(f) **Other Lease Provisions.** Although the Shared Lab Area does not form a part of the Premises, the provisions of this Lease (A) governing Tenant's use, operation, and enjoyment of the Premises, (B) imposing obligations on Tenant for matters occurring in, on, within, or about the Premises or arising out of the use or occupancy of the Premises (including, but not limited to, those obligations relating to insurance, indemnification, Hazardous Materials Clearance, and environmental requirements triggered by Tenant's use of the Shared Lab Area), and (C) limiting Landlord's liability, shall apply with equal force to Tenant's use of the Shared Lab Area and the Shared Lab Systems.

(g) **Termination.** If Tenant Defaults in its obligations under this Section 46, Landlord shall have the right, in addition to any other rights and remedies available to Landlord for a Default by Tenant, to terminate immediately Tenant's license to use the Shared Lab Area. The expiration or earlier termination of this Lease shall automatically terminate the license hereby granted to Tenant to so use the Shared Lab Area.

(h) **Shared Lab Area Operating Expenses.**

(i) **Shared Lab Area Operating Expense Payments.** Landlord shall deliver to Tenant an Annual Estimate of Operating Expenses (SLA) for each calendar year during the Term, which may be revised by Landlord from time to time during such calendar year. During each month of the Term, on the same date that Base Rent is due, Tenant shall pay Landlord, as Additional Rent hereunder, an amount equal to 1/12th of Tenant's Share (SLA) of the Annual Estimate of Operating Expenses (SLA). Payments for any fractional calendar month shall be prorated based on the number of days in the applicable month.

(ii) The term "**Operating Expenses (SLA)**" means all costs and expenses of maintaining, repairing, replacing and operating the Shared Lab Area and the Shared Lab Systems incurred or accrued each calendar year by Landlord.

(iii) Each Annual Statement shall include (a) the total and Tenant's Share (SLA) of actual Operating Expenses (SLA) for the previous calendar year and (b) the total of Tenant's payments in respect of Tenant's Share (SLA) of actual Operating Expenses (SLA) for such year. If Tenant's Share (SLA) of actual Operating Expenses (SLA) for such year exceeds Tenant's payments of Tenant's Share (SLA) of Operating Expenses (SLA) for such year, then the excess shall be due and payable by Tenant as Rent within 30 days after delivery of such Annual Statement to Tenant. If Tenant's payments of Operating Expenses (SLA) for such year exceed Tenant's Share (SLA) of actual Operating Expenses (SLA) for such year, then Landlord shall pay the excess to Tenant within 30 days after delivery of such Annual Statement, except that after the expiration, or earlier termination of the Term or if Tenant is delinquent in its obligation to pay Rent, Landlord shall pay the excess to Tenant after deducting all other amounts due Landlord. Operating Expenses (SLA) for the calendar years in which Tenant's obligation to share therein begins and ends shall be prorated.

47. **Miscellaneous.**

(a) **Notices.** All notices or other communications between the parties shall be in writing and shall be deemed duly given upon delivery or refusal to accept delivery by the addressee thereof if delivered in person, or upon actual receipt if delivered by reputable overnight guaranty courier, addressed and sent to the parties at their addresses set forth above. Landlord and Tenant may from time to time by written notice to the other designate another address for receipt of future notices.

(b) **Joint and Several Liability.** If and when included within the term “**Tenant**,” as used in this instrument, there is more than one person or entity, each shall be jointly and severally liable for the obligations of Tenant.

(c) **Financial Information.** Tenant shall furnish Landlord with true and complete copies of (i) Tenant’s most recent audited annual financial statements within 90 days of the end of each of Tenant’s fiscal years during the Term, (ii) Tenant’s most recent unaudited quarterly financial statements within 45 days of the end of each of Tenant’s first three fiscal quarters of each of Tenant’s fiscal years during the Term, (iii) at Landlord’s request from time to time, updated business plans, including cash flow projections and/or pro forma balance sheets and income statements, all of which shall be treated by Landlord as confidential information belonging to Tenant, (iv) corporate brochures and/or profiles prepared by Tenant for prospective investors, and (v) any other financial information or summaries that Tenant typically provides to its lenders or shareholders.

(d) **Recordation.** Neither this Lease nor a memorandum of lease shall be filed by or on behalf of Tenant in any public record. Landlord may prepare and file, and upon request by Landlord Tenant will execute, a memorandum of lease. Each such memorandum shall include such matters as may be required by the Register of New York County or Section 291-c of the Real Property Law of the State of New York to be included therein so as to permit the same to be recorded.

(e) **Interpretation.** The normal rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of this Lease or any exhibits or amendments hereto. Words of any gender used in this Lease shall be held and construed to include any other gender, and words in the singular number shall be held to include the plural, unless the context otherwise requires. The captions inserted in this Lease are for convenience only and in no way define, limit or otherwise describe the scope or intent of this Lease, or any provision hereof, or in any way affect the interpretation of this Lease.

(f) **Not Binding Until Executed.** The submission by Landlord to Tenant of this Lease shall have no binding force or effect, shall not constitute an option for the leasing of the Premises, nor confer any right or impose any obligations upon either party until execution of this Lease by both parties.

(g) **Limitations on Interest.** It is expressly the intent of Landlord and Tenant at all times to comply with applicable law governing the maximum rate or amount of any interest payable on or in connection with this Lease. If applicable law is ever judicially interpreted so as to render usurious any interest called for under this Lease, or contracted for, charged, taken,

reserved, or received with respect to this Lease, then it is Landlord's and Tenant's express intent that all excess amounts theretofore collected by Landlord be credited on the applicable obligation (or, if the obligation has been or would thereby be paid in full, refunded to Tenant), and the provisions of this Lease immediately shall be deemed reformed and the amounts thereafter collectible hereunder reduced, without the necessity of the execution of any new document, so as to comply with the applicable law, but so as to permit the recovery of the fullest amount otherwise called for hereunder.

(h) **Time.** Time is of the essence as to the performance of Tenant's obligations under this Lease.

(i) **Incorporation by Reference.** All exhibits and addenda attached hereto are hereby incorporated into this Lease and made a part hereof. If there is any conflict between such exhibits or addenda and the terms of this Lease, such exhibits or addenda shall control.

**48. Landlord Consent.**

(a) If, pursuant to the terms of this Lease, any consent or approval by Landlord or Tenant is not to be unreasonably withheld or is subject to a specified standard, then in the event of a final determination that the consent or approval was unreasonably withheld or that such specified standard has been met (such that the consent or approval should have been granted), the consent or approval shall be deemed granted but the granting of the consent or approval shall be the only remedy to the party requesting or requiring the consent or approval.

(b) If any matter which is the subject of a request for consent or approval hereunder by Tenant requires the consent or approval by any Superior Party under the Superior Instruments (including, by way of example, proposed Alterations), Tenant shall submit in writing such request (together with any plans, specifications or other materials or documents necessary or appropriate in connection therewith) to Landlord, and Landlord shall, provided Tenant is not then in monetary or material non-monetary default hereunder, in each instance, beyond the expiration of any applicable notice "and/or cure period, promptly forward such request to such of the foregoing parties from whom consent is required and otherwise cooperate reasonably with Tenant in requesting and seeking to obtain such required consent; and, in any such case, Landlord shall in no event be deemed to have unreasonably withheld or delayed any such request for consent or approval if any of the foregoing parties shall fail to respond to such request (unless such failure is deemed to constitute consent under the applicable Superior Instrument) or shall deny same. If Landlord shall so determine that any such matter requires the consent or approval of any of the foregoing parties, Landlord shall use good faith reasonable efforts to obtain from such parties such consent or approval (but without any obligation to pay any fee to such party unless Tenant agrees to pay the same); provided that Tenant shall submit to Landlord, upon Landlord's request therefor, all plans, specifications or other materials, information or documentation as may be reasonably required by such parties, under the Superior Instruments in connection with each such parties' respective consideration of such request. Tenant shall pay to Landlord, within thirty (30) days after demand therefor, as Additional Rent, all actual out-of-pocket fees, charges or other expenses Landlord may incur arising out of any such request for consent or approval. In no event shall Tenant communicate (other than through Landlord) with any Superior Party in respect of any Alterations or any other matter pertaining to this Lease.

49. **Hazardous Activities.** Notwithstanding any other provision of this Lease, Landlord, for itself and its employees, agents and contractors, reserves the right to refuse to perform any repairs or services in any portion of the Premises which, pursuant to Tenant's routine safety guidelines, practices or custom or prudent industry practices, require any form of protective clothing or equipment other than safety glasses. In any such case, Tenant shall contract with parties who are acceptable to Landlord, in Landlord's reasonable discretion, for all such repairs and services, and Landlord shall, to the extent required, equitably adjust Tenant's Share of Operating Expenses in respect of such repairs or services to reflect that Landlord is not providing such repairs or services to Tenant.

50. **Internet Service.** It is currently anticipated that wireless internet service ("**Internet Service**") will be available in the Common Areas and Open Space in the Project. In the event that Internet Service is so available, Tenant shall have the right, on a non-exclusive basis in common with other tenants and users of the Project, to use such Internet Service, subject to the further terms of this Section 50.

(a) Tenant acknowledges that Landlord is not the generator of Internet Service and that the availability and quality of Internet Service consequently is subject to the provision of the same to the Project by the third party provider(s) responsible for delivering same to the Project. Landlord shall have no liability for the availability, capacity, quality, continuity or character of service of Internet Service, and no abatement of Rent or other penalty shall arise due to, nor shall Landlord have any liability due to any loss, cost, claim, damage or expense arising from the availability, capacity, quality, continuity or character of service of Internet Service or any interruption, deterioration or removal of Internet Service. Tenant acknowledges that the capacity of Internet Service available for use by Tenant (if any) is part of the overall capacity of Internet Service available to the Project for use on a non-exclusive basis in common with all other tenants at the Project. Tenant agrees to limit Tenant's use of Internet Service to Tenant's reasonable share of the then-existing capacity of Internet Service, and Tenant shall not use Internet Service in a manner that interferes with any other tenant's or user's use of such Internet Service.

(b) By accessing or using Internet Service, Tenant accepts and agrees to comply with all terms and conditions applicable thereto (including any modifications and/or additions thereto provided in connection with accessing or using Internet Service from time to time).

(c) Tenant acknowledges and agrees that all information (including, without limitation, data files, written text, computer software, music, audio files or other sounds, photographs, graphics, videos or other images) which Tenant may have access to as a part of, or through Tenant's use of, Internet Service (collectively, "**Content**") is the sole responsibility of the person from whom such Content originated. Tenant acknowledges and agrees that by using Internet Service, Tenant may be exposed to Content that Tenant may find offensive, indecent or objectionable, and Tenant uses the Internet Service at its own risk. Landlord and any third party provider(s) responsible for delivering Internet Service to the Project reserve the right (but shall have no obligation) to pre-screen, review, flag, filter, modify, refuse or remove any or all Content from the Internet Service. Landlord does not control the Content posted via the Internet Service and, as such, does not guarantee the accuracy, integrity, or quality of such Content. Under no circumstances shall Landlord or any Superior Parties be liable in any way for any Content, including, without limitation, any errors or omissions in any Content, or for any loss or damage arising out of or in connection with Tenant's use of the Internet Service (including, without limitation, damages for loss of use, lost profits or loss of data or information of any kind).



(d) Tenant is solely responsible for maintaining Tenant's account for the use of Internet Service, and Tenant is fully responsible for all activities that occur under Tenant's account and in connection with Tenant's use of the Internet Service. Tenant agrees to notify Landlord and any third party provider(s) responsible for delivering Internet Service to the Project immediately of any unauthorized use of Tenant's account or any other breaches of security of which Tenant becomes aware. Tenant is solely responsible for, and shall indemnify, defend, and hold harmless Landlord and the Superior Parties for, any Content created, uploaded, posted, emailed, transmitted, displayed or otherwise made available by Tenant via the Internet Service and for any and all consequences of Tenant's use of the Internet Service (including, without limitation, any loss or damage suffered by Landlord or any Superior Parties arising therefrom or in connection therewith).

(e) Tenant agrees not to use the Internet Service to:

(i) upload, post, email, transmit or otherwise make available any Content that is unlawful, harmful, threatening, abusive, harassing, tortious, defamatory, vulgar, obscene, libelous, invasive of another's privacy, hateful, or racially, ethnically or otherwise objectionable;

(ii) harm minors in any way;

(iii) impersonate any person or entity or falsely state or otherwise misrepresent Tenant's affiliation with a person or entity;

(iv) forge headers or otherwise manipulate identifiers in order to disguise the origin of any Content transmitted through the Internet Service;

(v) upload, post, email, transmit or otherwise make available any Content that Tenant does not have a right to make available under any law or under contractual or fiduciary relationships (such as inside information, proprietary and confidential information learned or disclosed as part of employment relationships or under nondisclosure agreements);

(vi) upload, post, email, transmit or otherwise make available any Content that infringes any patent, trademark, trade secret, copyright or other proprietary or intellectual property rights of any party;

(vii) upload, post, email, transmit or otherwise make available any unsolicited or unauthorized advertising, promotional materials, "junk mail," "spam," "chain letters," "pyramid schemes," or any other form of solicitation, except in those areas (such as shopping) that are designated for such purpose;

(viii) upload, post, email, transmit or otherwise make available any material that contains software viruses or any other computer code, files or programs designed to interrupt, destroy or limit the functionality of any computer software or hardware or telecommunications equipment;

(ix) disrupt the normal flow of dialogue, cause a screen to “scroll” faster than other users of the Internet Services are able to type, or otherwise act in a manner that negatively affects other users’ ability to engage in real time exchanges;

(x) interfere with or disrupt the Internet Services or servers or networks connected to the Internet Services, or disobey any requirements, procedures, policies or regulations of networks connected to the Internet Services, including using any device, software or routine to bypass our robot exclusion headers;

(xi) intentionally or unintentionally violate any applicable local, state, national or international law, including, but not limited to, regulations promulgated by the U.S. Securities and Exchange Commission, any rules of any national or other securities exchange, including, without limitation, the New York Stock Exchange, the American Stock Exchange or the NASDAQ, and any regulations having the force of law;

(xii) provide material support or resources (or to conceal or disguise the nature, location, source, or ownership of material support or resources) to any organization(s) designated by the United States government as a foreign terrorist organization pursuant to Section 219 of the Immigration and Nationality Act;

(xiii) “stalk” or otherwise harass another; or

(xiv) collect or store personal data about other users in connection with the prohibited conduct and activities set forth in clauses (i) through (xiii) above.

(f) Tenant acknowledges, consents to and agrees that Landlord and/or any third party provider(s) responsible for delivering Internet Service to the Project may access, preserve and disclose Tenant’s account information associated with the Internet Service if required to do so by applicable Legal Requirements or in a good faith belief that such access, preservation or disclosure is reasonably necessary to (i) comply with legal process, (ii) comply with the directives of law enforcement officials, (iii) enforce the provisions of this Section 50 and/or the terms and conditions applicable to the Internet Service from time to time, (iv) respond to claims that any Content violates the rights of third parties, (v) respond to Tenant’s requests for customer service, and/or (vi) protect the rights, property or personal safety of Landlord, the Superior Parties, any third party provider(s) responsible for delivering Internet Service to the Project, any users of Internet Service, any tenants or other occupants of the Project and the public.

(g) Tenant acknowledges and agrees that the Internet Service may include security components that permit digital materials to be protected, and that the use of these materials is subject to such usage rules as may be set by Landlord, any third party provider(s) responsible for delivering Internet Service to the Project, and/or any Content provider(s). Tenant shall not attempt to override or circumvent any of such usage rules, and any unauthorized reproduction, publication, further distribution or public exhibition of the materials provided on the Internet Service, in whole or in part, is strictly prohibited.

IN WITNESS WHEREOF, Landlord and Tenant have executed this Lease as of the day and year first above written.

**TENANT:**

**MEIRAGTX, LLC,**  
a Delaware limited liability company

By: /s/ Rich Giroux

Its: Chief Operating Officer

**LANDLORD:**

**ARE-EAST RIVER SCIENCE PARK, LLC,**  
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,  
a Delaware limited partnership,  
managing member

By: ARE-QRS CORP.,  
a Maryland Corporation  
general partner

By: /s/ Gary Dean

Name: Gary Dean

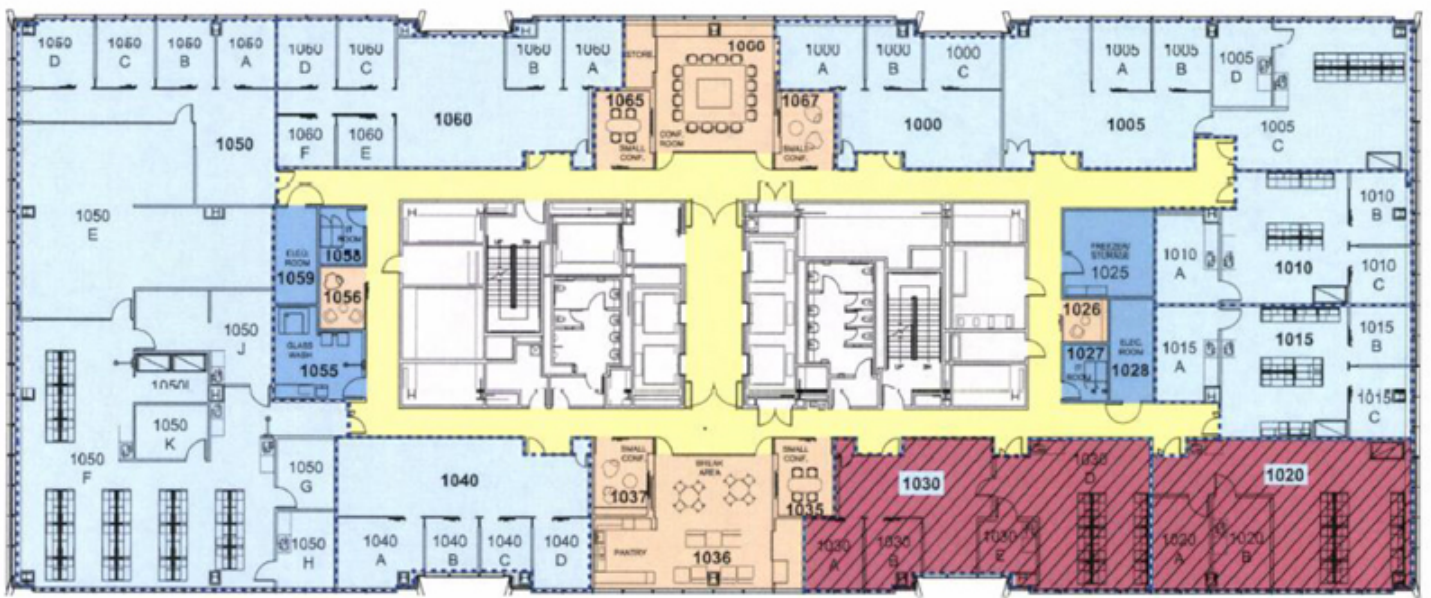
Its: Senior Vice President RE Legal Affairs

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**EXHIBIT A TO LEASE**

**DESCRIPTION OF PREMISES**

[See Attached]



**EXHIBIT B TO LEASE**

**DESCRIPTION OF PROJECT**

**PARCEL. OF LAND  
BEING NEW TAX LOT 99 IN TAX BLOCK 962  
IN THE BOROUGH OF MANHATTAN  
CITY OF NEW YORK  
NEW YORK COUNTY, NEW YORK**

All that certain plot, piece or parcel of land situate, lying and being In the Borough of Manhattan, City, County, and State of Now York, being more particularly bounded and described as follows:

**LOT 99 (PARCEL 3)**

BEGINNING at a point on the southerly side of former East 30th Street (60 feet side); said point being 416.74 feel distant easterly from the corner formed by the Intersection of the easterly side of First Avenue (100 feet wide) with the southerly side of former East 30<sup>th</sup> Street, discontinued and closed;

Running thence easterly along southerly side of former East 30th Street, discontinued and closed, a distance of 44.48 feet to a point;

Running thence southerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 154.73 feet to a point; said line forming an interior angle of 90 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence easterly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 208.30 feet to a point of curvature; said line forming an interior angle of 90 degrees 00 minutes 39 seconds with the last-mentioned course;

Running thence southeasterly through lands now or formerly Bellevue Hospital (tax Lot 100) on a curve bearing to the left with a radius of 166.00 feet and a central angle of 00 degrees 49 minutes 52 seconds, an arc distance of 2.26 feet to a point of tangential reverse curve; the northerly side of the radial line of said curve forming an angle of 160 degrees 06 minutes 40 seconds with the northerly side of the last mentioned course;

Running thence southeasterly through lands now or formerly Bellevue Hospital (tax Lot 100) on a curve bearing to the right side with a radius of 1823.85 feet and a central angle of 04 degrees 26 minutes 04 seconds, an arc distance of 142.22 feet to a point of compound curve;

Running thence southeasterly through lands now or formerly Bellevue Hospital (tax Lot 100) on a curve bearing to the right with a radius of 931.43 feet and a central angle of 03 degrees 09 minutes 25 seconds, an arc distance of 50.77 feet to a point of reverse curve;

Running thence southeasterly through lands now or formerly Bellevue Hospital (tax Lot 100), on a curve bearing to the left with a radius of 264.50 feet and a central angle of 02 degrees 27 minutes 42 seconds, an arc distance of 11.36 feet to a point;

Running thence southeasterly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 29.81 feet to a point; said line forming an exterior angle of 90 degrees 00 minutes 00 seconds with a radial line of the last-mentioned course;

Running thence southwesterly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 22.98 feet to a point; said line forming an interior angle of 89 degrees 09 minutes 05 seconds with the last-mentioned course;

Running thence southerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 12.82 feet to a point; said line forming an interior angle of 255 degrees 18 minutes 20 seconds with the last-mentioned course;

Running thence westerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 12.33 feet to a point; said line forming an interior angle of 90 degrees 01 minutes 30 seconds with the last-mentioned course;

Running thence southerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 7.95 feet to a point; said line forming an interior angle of 269 degrees 58 minutes 12 seconds with the last-mentioned course;

Running thence westerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 174.41 feet to a point; said line forming an interior angle of 90 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence northerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 53.17 feet to a point; said line forming an interior angle of 90 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence westerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 100.91 feet to a point; said line forming an interior angle of 270 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence westerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 141.75 feet to a point; said line forming an interior angle of 179 degrees 52 minutes 00 seconds with the last-mentioned course;

Running thence westerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 49.25 feet to a point; said line forming an interior angle of 180 degrees 08 minutes 00 seconds with the last-mentioned course;

Running thence southerly through land now or formerly of Bellevue Hospital (tax Lot 100), a distance of 0.60 feet to a point; said line forming an interior angle of 270 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence westerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 83.53 feet to a point; said line forming an interior angle of 90 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence northerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 102.83 feet to a point; said line forming an interior angle of 90 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence westerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 152.62 feet to a point on the easterly side of First Avenue; said line forming an interior angle of 270 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence northerly along with easterly side of First Avenue, a distance of 53.87 feet to a point; said line forming an interior angle of 90 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence easterly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 398.90 feet to a point of curvature, said line forming an interior angle of 90 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence northeasterly through lands now or formerly Bellevue Hospital (tax Lot 100) on a curve bearing to the left with a radius of 107.00 feet and a central angle of 02 degrees 56 minutes 57 seconds, an arc distance of 5.51 feet to a point, the radial line of said curve forming an exterior angle of 58 degrees 29 minutes 28 seconds with the last-mentioned course;

Running thence northeasterly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 16.46 feet to a point, said line forming an exterior angle of 90 degrees 00 minutes 00 seconds with the radial line of the last-mentioned course;

Running thence northerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 48.42 feet to a point, said line forming an interior angle of 233 degrees 32 minutes 31 seconds with the last-mentioned course;

Running thence easterly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 3.08 feet to a point, said line forming an interior angle of 90 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence northerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 76.00 feet to a point, said line forming an interior angle of 270 degrees 00 minutes 00 seconds with the last-mentioned course;

Running thence westerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 2.98 feet to a point, said line forming an interior angle of 270 degrees 00 minutes 00 seconds with the last-mentioned course;



Running thence northerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 61.14 feet, said line forming an interior angle of 90 degrees 00 minutes 00 seconds with the last-mentioned course to the place and point of beginning;

Together with the benefit of the easements set forth in that certain Temporary and Permanent Easement Agreement made between The City of New York, New York City Health and Hospitals Corporation and ARE-East River Science Park, LLC, dated December 29, 2006 to be recorded in the Office of the City Register, New York County.

THE FOLLOWING IS THE "OPTION LAND" UNDER THE GROUND LEASE, AND WILL BE INCLUDED IN THE "LAND" IF THE OPTION UNDER THE GROUND LEASE IS EXERCISED.

**A LEASE PARCEL OF LAND  
BEING A PORTION OF TAX LOT 100 IN TAX BLOCK 962  
IN THE BOROUGH OF MANHATTAN  
CITY OF NEW YORK  
NEW YORK COUNTY, NEW YORK**

All that certain plot, piece or parcel of land situate, lying in tax Block 962 as laid out on the Borough President of Manhattan Borough Survey Maps Nos. 34 and 39 and laid out on the Borough President of Manhattan Final Sectional Maps Nos. 44 and 45 and being a portion of tax Lot 100, Borough of Manhattan, City, County, and State of New York, being more particularly bounded and described as follows:

**PARCEL 2**

BEGINNING at a point on the southerly side of former East 30th Street (60 feet wide), discontinued and closed; said point have 461.22 feet distant from the corner formed by the Intersection of the easterly side of First Avenue with the southerly side of former East 30th Street (60 feet wide), discontinued and closed;

Running thence easterly along said southerly side of former East 30th Street, discontinued and closed, a distance of 156.64 feet to a point on the westerly side of Franklin D. Roosevelt Drive (width varies);

Running thence southerly along the westerly side of Franklin D. Roosevelt Drive, a distance of 0.02 feet to a point; said line forming an interior angle of 99 degrees 26 minutes 57 seconds with the last-mentioned course;

Running thence easterly along the westerly side of Franklin D. Roosevelt Drive, a distance of 10.10 feet to a point; said line forming an interior angle of 260 degrees 33 minutes 03 seconds with the last-mentioned course;

Running thence southeasterly through lands now or formerly Bellevue Hospital (tax Lot 100) on a curve bearing to the right with a radius of 24.00 feet and a central angel of 19 degrees 03 minutes 15 seconds, an arc distance of 7.98 feet to a point of tangent, the northerly side of the radial line of said curve forming an angle of 40 degrees 56 minutes 00 seconds with the southerly side of the last-mentioned course;

Running thence southeasterly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 42.30 feet to a point of curvature;

Running thence southerly on a curve bearing to the right with a radius of 144.00 feet and a central angle of 22 degrees 15 minutes 45 seconds, an arc distance of 55.95 feet to a point of reverse curve;

Running thence southerly through lands now or formerly Bellevue Hospital (tax Lot 100) on a curve bearing to the left with a radius of 156.00 feet and a central angle of 20 degrees 15 minutes 42 seconds, an arc distance of 55.17 feet to a point;

Running thence westerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 206.30 feet to a point; said line forming an angle of 160 degrees 08 minutes 40 seconds on its northerly side with the northerly side of the radial line of the last-mentioned course;

Running thence northerly through lands now or formerly Bellevue Hospital (tax Lot 100), a distance of 154.73 feet to the place and point of Beginning; said line forming an interior angle of 90 degrees 00 minutes 39 seconds with the last-mentioned course,

Containing 29,680.05 square feet or 0.6787 acre.

Together with a Construction and Permanent Easement Agreement and Exhibits.

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**EXHIBIT C TO LEASE**

**INTENTIONALLY OMITTED**

**EXHIBIT D TO LEASE**

**ACKNOWLEDGMENT OF COMMENCEMENT DATE**

This **ACKNOWLEDGMENT OF COMMENCEMENT DATE** is made as of this \_\_\_\_\_ day of \_\_\_\_\_, 20\_\_\_\_, between ARE-East River Science Park, LLC a Delaware limited liability company ("**Landlord**"), and MeiraGTx, LLC, a Delaware limited liability company ("**Tenant**"), and is attached to and made a part of that certain Lease Agreement, dated as of \_\_\_\_\_, 20\_\_\_\_, (the "**Lease**"), by and between Landlord and Tenant. Any initially capitalized terms used but not defined herein shall have the meanings given them in the Lease.

Landlord and Tenant hereby acknowledge and agree, for all purposes of the Lease, that the Commencement Date of the Base Term of the Lease is \_\_\_\_\_, 20\_\_\_\_ and the termination date of the Base Term of the Lease shall be midnight on \_\_\_\_\_, 20\_\_\_\_. In case of a conflict between this Acknowledgment of Commencement Date and the Lease, this Acknowledgment of Commencement Date shall control for all purposes.

IN WITNESS WHEREOF, Landlord and Tenant have executed this **ACKNOWLEDGMENT OF COMMENCEMENT DATE** to be effective on the date first above written.

**TENANT:**

**MeiraGTx, LLC,**  
a Delaware limited liability company

By: \_\_\_\_\_  
Name: \_\_\_\_\_  
Its: \_\_\_\_\_

**LANDLORD:**

**ARE-EAST RIVER SCIENCE PARK, LLC,**  
a Delaware limited liability company

By: **ALEXANDRIA REAL ESTATE EQUITIES, L.P.,**  
a Delaware limited partnership,  
managing member

By: **ARE-QRS CORP.,**  
a Maryland corporation,  
general partner

By: \_\_\_\_\_  
Name: \_\_\_\_\_  
Its: \_\_\_\_\_

**EXHIBIT E TO LEASE**

**RULES AND REGULATIONS**

1. The sidewalks, entries, and driveways of the Project shall not be obstructed by Tenant, or any Tenant Party, or used by them for any purpose other than ingress and egress to and from the Premises.
2. Tenant shall not place any objects, including antennas, outdoor furniture, etc., in the parking areas, landscaped areas or other areas outside of its Premises, or on the roof of the Project.
3. Except for animals assisting the disabled, no animals shall be allowed in the offices, halls, or corridors in the Project.
4. Tenant shall not disturb the occupants of the Project or adjoining buildings by the use of any radio or musical instrument or by the making of loud or improper noises.
5. If Tenant desires telegraphic, telephonic or other electric connections in the Premises, Landlord or its agent will direct the electrician as to where and how the wires may be introduced; and, without such direction, no boring or cutting of wires will be permitted. Any such installation or connection shall be made at Tenant's expense.
6. Tenant shall not install or operate any steam or gas engine or boiler, or other mechanical apparatus in the Premises, except as specifically approved in the Lease. The use of oil, gas or inflammable liquids for heating, lighting or any other purpose is expressly prohibited. Explosives or other articles deemed extra hazardous shall not be brought into the Project.
7. Parking any type of recreational vehicles is specifically prohibited on or about the Project. Except for the overnight parking of operative vehicles, no vehicle of any type shall be stored in the parking areas at any time. In the event that a vehicle is disabled, it shall be removed within 48 hours. There shall be no "For Sale" or other advertising signs on or about any parked vehicle. All vehicles shall be parked in the designated parking areas in conformity with all signs and other markings. All parking will be open parking, and no reserved parking, numbering or lettering of individual spaces will be permitted except as specified by Landlord.
8. Tenant shall maintain the Premises free from rodents, insects and other pests.
9. Landlord reserves the right to exclude or expel from the Project any person who, in the judgment of Landlord, is intoxicated or under the influence of liquor or drugs or who shall in any manner do any act in violation of the Rules and Regulations of the Project.
10. Tenant shall not cause any unnecessary labor by reason of Tenant's carelessness or indifference in the preservation of good order and cleanliness. Landlord shall not be responsible to Tenant for any loss of property on the Premises, however occurring, or for any damage done to the effects of Tenant by the janitors or any other employee or person.

11. Tenant shall give Landlord prompt notice of any defects in the water, lawn sprinkler, sewage, gas pipes, electrical lights and fixtures, heating apparatus, or any other service equipment affecting the Premises.
12. Tenant shall not permit storage outside the Premises, including without limitation, outside storage of trucks and other vehicles, or dumping of waste or refuse or permit any harmful materials to be placed in any drainage system or sanitary system in or about the Premises.
13. All moveable trash receptacles provided by the trash disposal firm for the Premises must be kept in the trash enclosure areas, if any, provided for that purpose.
14. No auction, public or private, will be permitted on the Premises or the Project.
15. No awnings shall be placed over the windows in the Premises except with the prior written consent of Landlord.
16. The Premises shall not be used for lodging, sleeping or cooking or for any immoral or illegal purposes or for any purpose other than that specified in the Lease. No gaming devices shall be operated in the Premises.
17. Tenant shall ascertain from Landlord the maximum amount of electrical current which can safely be used in the Premises, taking into account the capacity of the electrical wiring in the Project and the Premises and the needs of other tenants, and shall not use more than such safe capacity. Landlord's consent to the installation of electric equipment shall not relieve Tenant from the obligation not to use more electricity than such safe capacity.
18. Tenant assumes full responsibility for protecting the Premises from theft, robbery and pilferage.
19. Tenant shall not install or operate on the Premises any machinery or mechanical devices of a nature not directly related to Tenant's ordinary use of the Premises and shall keep all such machinery free of vibration, noise and air waves which may be transmitted beyond the Premises.
20. Landlord reserves the right to exclude any individuals from the Project at any time in its sole and absolute discretion. Tenant acknowledges this right and agrees to cooperate with Landlord, subject to applicable law, in Landlord's exercise of this right.

**EXHIBIT F TO LEASE**

**TENANT'S PERSONAL PROPERTY**

None except as set forth below:

None.

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**EXHIBIT G TO LEASE**

**[INTENTIONALLY OMITTED]**



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**EXHIBIT H TO LEASE**

**[INTENTIONALLY OMITTED]**

**EXHIBIT I TO LEASE**

**SHARED LAB SYSTEMS**

**10<sup>th</sup> Floor Science Hotel:**

- Built-in Laboratory Sterilizer.
- Built-in Glassware Washers.
- Shared Vacuum system located in 7th Floor Mechanical Room.
- Shared compressed air system located in 7th Floor Mechanical Room.
- Shared RO/DI water system located in 7th Floor Mechanical Room.

**EXHIBIT J TO LEASE**

**ADDITIONAL INSUREDS**

The East River Science Park Condominium

Alexandria Real Estate Equities, Inc.

New York City Health and Hospitals Corporation

New York City Economic Development Corporation

New York City Industrial Development Agency

City of New York

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**EXHIBIT K TO LEASE**

**[INTENTIONALLY OMITTED]**

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**EXHIBIT L TO LEASE**

**OPEN SPACE DESCRIPTION**

EXHIBIT L-1



PHASE II  
PHASE I

FOR DRIVE

12.15'

COTTON PARCEL  
(PROPOSED NORTH TOWER)

LINE OF LOWEST BELOW  
CONFLUENCE

EAST TOWER

WINTER  
GARDEN

WINTER  
GARDEN  
BRIDGE

CONTINUED ACCESS TO AND FROM  
MILL AVENUE AT ALL TIMES DURING  
SPECIAL / SPONSORED EVENTS

30TH ST

FIRST AVENUE

WEST TOWER

LEGEND

-  PUBLICLY ACCESSIBLE OPEN SPACE- PLAZA
-  PROPOSED BUILDING
-  SPECIAL / SPONSORED EVENT AREA (16,145 SF)

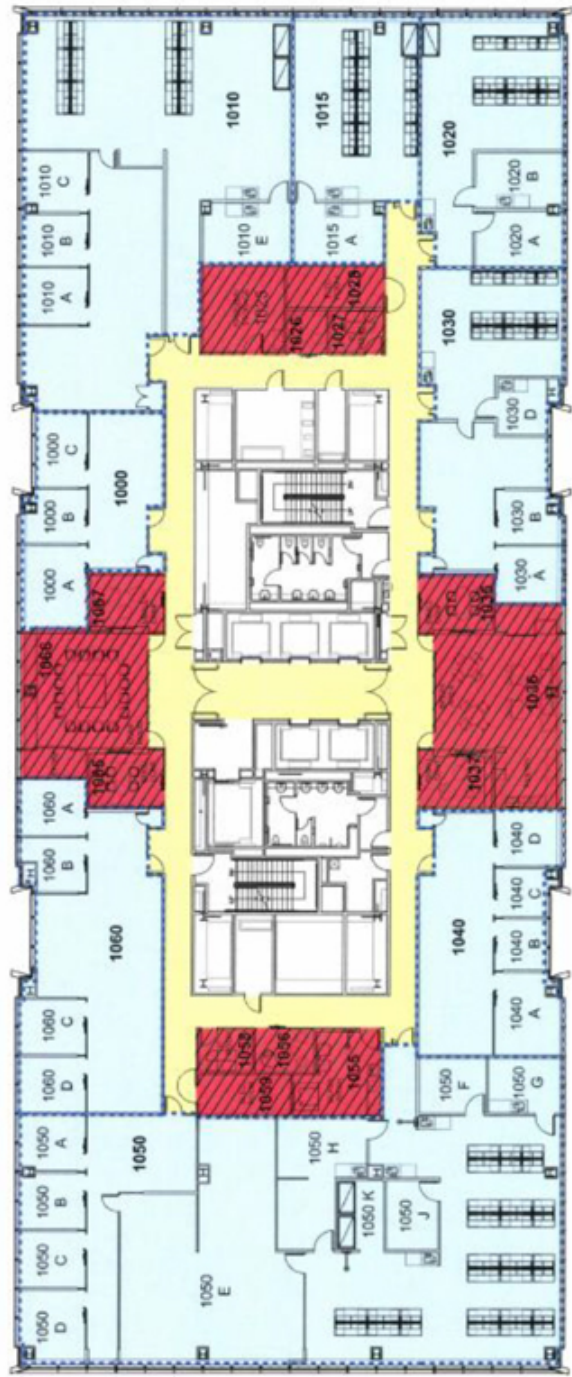
PUBLICLY ACCESSIBLE OPEN SPACE

- PHASE I: NOT LESS THAN 48,800 SF
- PHASE II: NOT LESS THAN 14,400 SF
- TOTAL: 61,000 SF



CONFIDENTIAL AND PROPRIETARY

EXHIBIT L



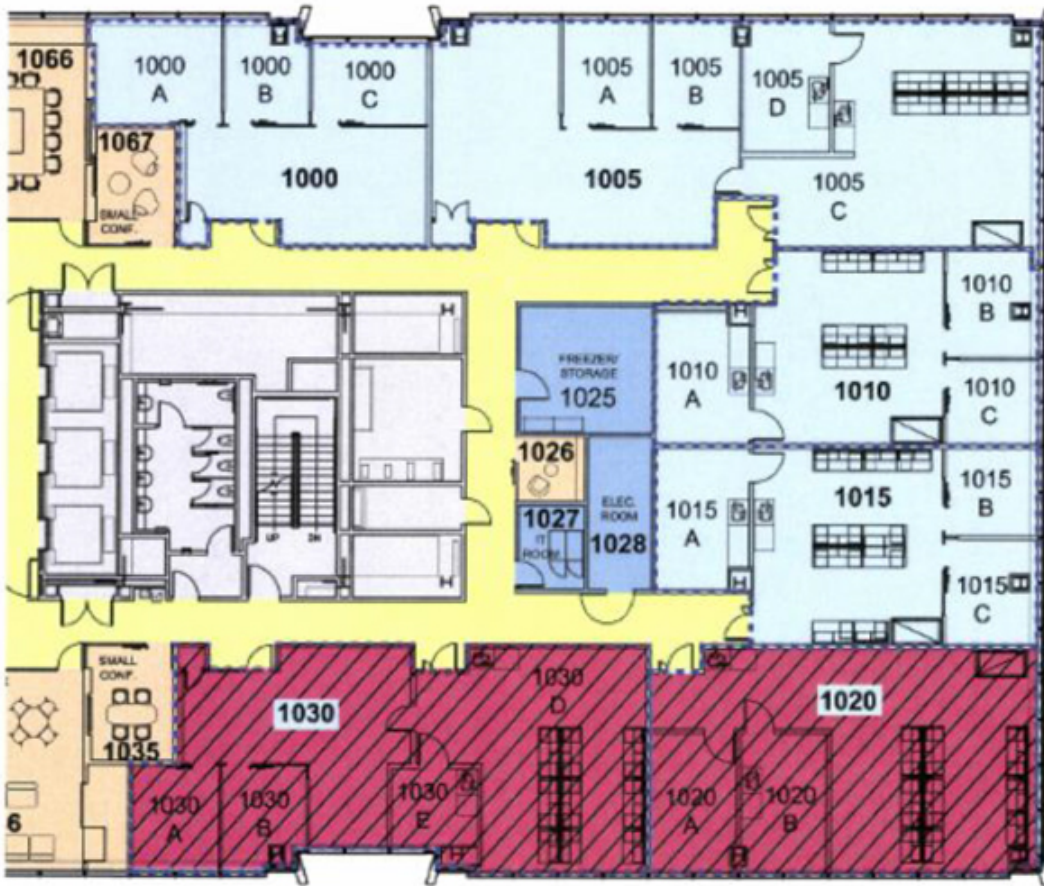


Exhibit A

*\*\*Suite 1030 does not include a chemical fume hood\*\**



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**EXHIBIT M TO LEASE**

**SUPERIOR INSTRUMENT EXCERPTS**

Exhibit M-1

## LEASE AGREEMENT

This LEASE AGREEMENT, made and entered into as of December 1, 2006 (this "Agreement"), by and between NEW YORK CITY INDUSTRIAL DEVELOPMENT AGENCY, a corporate governmental agency constituting a body corporate and politic and a public benefit corporation of the State of New York, duly organized and existing under the laws of the State of New York (the "Agency"), having its principal office at 110 William Street New York, New York 10038, party of the first part, and ARE-EAST RIVER SCIENCE PARK, LLC, a limited liability company duly organized and existing under the laws of the State of Delaware (the "Lessee"), having its principal office at 385 East Colorado Boulevard, Suite 299, Pasadena, California 91101, party of the second part;

### WITNESSETH:

WHEREAS, the New York State Industrial Development Agency Act, constituting Title 1 of Article 18-A of the General Municipal Law, Chapter 24 of the Consolidated Laws of New York, as amended (the "Enabling Act"), authorizes and provides for the creation of industrial development agencies in the several counties, cities, villages and towns in the State of New York and empowers such agencies, among other things, to acquire, construct, reconstruct, lease, improve, maintain, equip and furnish land, any building or other improvement, and all real and personal properties, including but not limited to machinery and equipment, deemed necessary in connection therewith, whether or not now in existence or under construction, which shall be suitable for manufacturing, warehousing, research, commercial, industrial or civic purposes, to the end that such agencies may be able to promote, develop, encourage, assist and advance the job opportunities, health, general prosperity and economic welfare of the people of the State of New York and to improve their prosperity and standard of living; and

WHEREAS, pursuant to and in accordance with the provisions of the Enabling Act, the Agency was established by Chapter 1082 of the 1974 Laws of New York, as amended (together with the Enabling Act, the "Act"), for the benefit of The City of New York (the "City") and the inhabitants thereof; and

WHEREAS, pursuant to a certain Agreement of Lease, dated as of December 29, 2006 (as the same has been and may hereafter be amended, supplemented or assigned, the "Ground Lease"), between the New York City Health and Hospitals Corporation, as landlord ("HHC"), and foe Lessee, as tenant, HHC wishes to lease the hereinbelow defined Land to the Lessee for the development of a commercial bioscience and scientific research and development facility in furtherance of tile City's goal of creating additional space in the City for commercial bioscience companies; and

WHEREAS, to accomplish the purposes of the Act, the Agency has entered into negotiations with the Lessee, an affiliate of Alexandria Real Estate Equities, Inc. (the "Company"), for the development of the East River Science Park. a commercial bioscience park, on an approximately 2.8 acre site located between East 28th and East 30th Streets and First Avenue and the FDR Drive in the Borough of Manhattan (collectively, the "Land"), and otherwise described in Exhibit A – "Description of Land" – attached hereto and made a part hereof; and

WHEREAS, the project will consist of the construction and equipping of two lab/office towers on the Land (the "Facility"), totaling approximately 541,000 square feet, which buildings will primarily provide lab and related office space for commercial bioscience companies, and will also include a café, a conference center, street-level retail, and office space for bioscience venture capital firms, and over an acre of publicly accessible open space (the "Project"); and

Text Redacted by a third party and not known to Registrant

An Affiliate of a Person shall mean a Person that directly or indirectly through one or more intermediaries controls, or is under common control with, or is controlled by, such Person. The term "control" (including the related terms "controlled by" and "under common control with") means (i) the possession, directly or indirectly, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise, and (ii) the ownership, either directly or indirectly, of at least 51% of the voting stock or other equity interest of such Person.

Agency shall mean the New York City Industrial Development Agency, a corporate governmental agency constituting a body corporate and politic and a public benefit corporation of the State, duly organized and existing under the laws of the State, and any body, board, authority, agency or other governmental agency or instrumentality which shall hereafter succeed to the powers, duties, obligations and functions thereof.

Agreement shall mean this Lease Agreement, between the Agency and the Lessee, and shall include any and all amendments hereof and supplements hereto hereafter made in conformity herewith.

Text Redacted by a third party and not known to Registrant

Authorized Representative shall mean, (i) in the case of the Agency, the Chairperson, Vice Chairperson, Treasurer, Assistant Treasurer, Secretary, Assistant Secretary, Executive Director, Deputy Executive Director, General Counsel or Vice President for Legal Affairs of the Agency, or any other officer or employee of the Agency who is authorized to perform specific acts or to discharge specific duties hereunder and of whom another Authorized Representative of the Agency has given written notice to the Lessee; and (ii) in the case of the Lessee, any member or any other employee who is authorized to perform specific acts or to discharge specific duties hereunder and of whom another Authorized Representative of the Lessee has given written notice to the Agency.

Background Investigative Check shall mean the due diligence performed with the background investigative report then in current use by The City of New York.

Text Redacted by a third party and not known to Registrant

City shall mean The City of New York, New York.

Text Redacted by a third party and not known to Registrant

Company shall mean Alexandria Real Estate Equities, Inc., a Maryland corporation, and its permitted successors and assigns.

Text Redacted by a third party and not known to Registrant

Facility shall mean, collectively, the Land and the improvements.

Text Redacted by a third party and not known to Registrant

Ground Lease shall have the meaning set forth in the recitals hereto.

Text Redacted by a third party and not known to Registrant

Improvements shall mean all buildings, structures, foundations, related facilities, fixtures and other improvements existing on the Commencement Date or at any time made, erected or situated on the Land (including any improvements made as part of the Project pursuant to Section 2.2 hereof) and all replacements, improvements, extensions, substitutions, restorations, repairs or additions thereto (other than those improvements in space occupied by a Tenant which, pursuant to the related Tenant Lease, is owned by such Tenant); provided, however, that the Improvements shall not include those improvements in a space occupied by a municipality as defined in the Section 854(3) of the General Municipal Law of the State.

Text Redacted by a third party and not known to Registrant

Land shall mean those certain lots, pieces or parcels of land located between East 28th and East 30th Streets and First Avenue and the FDR Drive in the Borough of Manhattan within the Bellevue Hospital Center Campus and designated as Block 962, Lot 99, all as more particularly described in Exhibit A – “Description of the Land” hereto, which is made a part hereof, together with all easements, rights and interests now or hereafter appurtenant or beneficial thereto; but excluding, however, any real property or interest therein released pursuant to Section 6.4 hereof and any real property or interests therein being leased to or reserved for use by a municipality as defined in the Section 854(3) of the General Municipal Law of the State.

Text Redacted by a third party and not known to Registrant

Lessee shall mean ARE-East River Science Park, LLC, a Delaware limited liability company, and its permitted successors and assigns pursuant to Sections 6.1 or 9.3 hereof.

Text Redacted by a third party and not known to Registrant

Major Tenant shall mean a Tenant subject to a Major Tenant Lease.

Major Tenant Lease shall mean any and all Tenant Leases that are for at least five (5) full floors or the equivalent of five (5) full average floors at the Project. For purposes of determining whether a Tenant Lease is a Major Tenant Lease, any expansion rights of the Tenant shall be taken into account as if exercised in determining the rentable area leased by such Tenant.

Text Redacted by a third party and not known to Registrant

Person shall mean any individual, corporation, partnership, joint venture, association, joint stock company, trust, unincorporated organization, general partnership, limited liability company or government or any agency or political subdivision thereof or other entity.

Text Redacted by a third party and not known to Registrant

Prohibited Person shall mean (i) any Person (A) that is in default or in breach, beyond any applicable grace period, of its obligations under any written agreement with the Agency or the City, or (B) that directly or indirectly controls, is controlled by, or is under common control with a Person that is in default or in breach, beyond any applicable grace period, of its obligations under any written agreement with the Agency or the City, unless such default or breach has been waived in writing by the Agency or the City, as the case may be, and (ii) any Person (A) that has been convicted in a criminal proceeding for a felony or any crime involving moral turpitude or that is an organized crime figure or is reputed to have substantial business or other affiliations with an organized crime figure, or (B) that directly or indirectly controls, is controlled by, or is under common control with, a Person that has been convicted for a criminal proceeding for a felony or any crime involving moral turpitude or that is an organized crime figure or is reputed to have substantial business or other affiliations with an organized crime figure.

Project shall have the meaning ascribed thereto in the recitals hereto.

State shall mean the State of New York.

Tenant shall mean any Person who shall lease, use or occupy any portion of the Facilities pursuant to a Tenant Lease.

Tenant Lease shall mean any lease or sublease, including any Major Tenant Lease, by the Lessee (or by any other Person whose leasehold estate in the Facility or any portion thereof is derivative of the Lessee) of property constituting all or say part of the Facility, any tenancy with respect to the Facility or any part thereof, whether or not in writing, any license or concession agreement and any other agreement, by whatever name called, involving a transfer or creation of possessory rights or similar rights of use or occupancy, in the Facility or any part thereof without transfer of title, and any and all guarantees of any of the foregoing, whether now existing or hereafter made; provided, however, any assignment by a Tenant of a Tenant Lease by the existing Tenant to a new Person shall be deemed a new Tenant Lease.

Section 6.9 Employment Information, Opportunities and Guidelines. (A) The Lessee agrees to submit to the Agency on August 1st of each year a completed Employment and Benefits Report in the form of Schedule B – “Employment and Benefits Report” attached hereto to the extent that the Lessee shall have received Financial Assistance (as such term is defined in the Employment and Benefits Report) from the Agency during the twelve-month period ending on the June 30th immediately preceding such August 1st. In addition, upon termination of this Agreement, the Lessee shall submit to the Agency an employment report with respect to both the Lessee and, where so stated, the Tenants, substantially in the form of Schedule B hereto, certified as to accuracy by an Authorized Representative of the Lessee, and shall attach thereto a copy of the Lessee’s final payroll report evidencing the total number of employees employed by the Lessee during the most recent period commencing July 1 of the previous year and ending June 30 of the year of the obligation of filing such report. Annually, by July 31 of each year, commencing on July 1, 2007, until the termination of this Agreement, the Lessee shall submit to the Agency the contact and location report substantially in the form attached hereto as Schedule C.

(a) The Lessee shall ensure that all employees and applicants for employment with the Lessee with regard to the Facility are afforded equal employment opportunities without discrimination. Except as is otherwise provided by collective bargaining contracts or agreements, new employment opportunities created at the Lessee as a result of the Project shall be listed with the New York State Department of Labor Community Services Division, and with the administrative entity of the service delivery area created by the Workforce Investment Act of 1998 (P.L. No. 105-220) in which the Facility is located. Except as is otherwise provided by collective bargaining contracts or agreements, the Lessee agrees, where practicable, to consider first, and cause each of its Affiliates at the Facility to consider first, persons eligible to participate in the Workforce Investment Act of 1998 (P.L. No. 105-220) programs who shall be referred by administrative entities of service delivery areas created pursuant to such act or by the Community Services Division of the New York State Department of Labor for such new employment opportunities.

(b) The Lessee hereby authorizes any private or governmental entity, including but not limited to The New York State Department of Labor (“DOL”), to release to the Agency and/or the New York City Economic Development Corporation (“EDC”), and/or to the successors and assigns of either (collectively, the “Information Recipients”), any and all employment information under its control and pertinent to the Lessee and the employees of the Lessee to enable the Agency and/or EDC to comply with its reporting requirements required by New York City Local Law 48 of 2005 and any other applicable laws, rules or regulations. In addition, upon the Agency’s written request, the Lessee shall provide to the Agency any employment information in the possession of the Lessee which is pertinent to the Lessee and the employees of the Lessee to enable the Agency and/or EDC to comply with its reporting requirements required by New York City Local Law 48 of 2005 and any other applicable laws, rules or regulations. Information released or provided to Information Recipients by DOL, or by any other governmental entity, or by any private entity, or by the Lessee, or any information previously released as provided by all or any of the foregoing parties (collectively, “Employment Information”) may be disclosed by the Information Recipients in connection with the administration of the programs of the Agency, and/or EDC, and/or the successors and assigns of either, and/or The City of New York, and/or as may be necessary to comply with law; and, without limiting the foregoing, the Employment Information may be included in (x) reports prepared by the Information Recipients pursuant to New York City Local Law 48 of 2005, (y) other reports required of the Agency, and (z) any other reports required by law. This authorization shall remain in effect throughout the term of this Agreement.

(c) Nothing in this Section shall be construed to require the Lessee to violate any existing collective bargaining agreement with respect to hiring new employees.

(d) Additionally, the Lessee shall submit to the Agency, together with Schedule B referred to above, a letter of representation that there are no existing tenants at the Project other than the Lessee and tenants authorized pursuant to this Agreement and the Ground Lease.

Text Redacted by a third party and not known to Registrant

Section 6.13 Subtenant Survey. The Lessee shall file with the Agency by January 1 and July 1 of each year, commencing January 1, 2007, a certificate of an Authorized Representative of the Lessee with respect to all subtenancies in effect at the Facility, in the form attached hereto as Schedule D.

Text Redacted by a third party and not known to Registrant

(ii) Promptly following the execution of each Tenant Lease, the Lessee shall deliver to the Agency:

(1) written notice of such Tenant Lease setting forth the name of the Tenant, the square footage of the Facility which shall be demised under such Tenant Lease, the intended use of the demised premises, and the term of such Tenant Lease (including any renewal options);

(2) a certificate of an Authorized Representative of the Lessee to the effect that, to the best of its knowledge, and based in part upon a representation of such Tenant, either (A) such Tenant's occupancy of the Facility will not result in the removal of a plant or facility of such Tenant located outside of the City (but within the State) to the Facility or in the abandonment of one or more of such plants or facilities of such Tenant located outside of the City (but within the State), or (B) such Tenant's location at the Facility is reasonably necessary to discourage such Tenant from removing its business to a location outside of the State or is reasonably necessary to preserve such Tenant's competitive position in its industry;

(3) a certificate of an Authorized Representative of the Lessee to the effect that the Tenant Lease obligates the Tenant to timely provide to the Lessee the information that the Lessee needs in order to satisfy the reporting requirements of the Lessee under Sections 6.9 end 6.13 hereof and Sections 92(b)(ii)(2) and 9.2(b)(ii)(4) hereof; and

(4) a certificate of the Authorized Representative of the Lessee to the effect that, to the best of its knowledge, and based in part upon a representation of such Tenant, neither such Tenant, nor any Person which controls such Tenant, nor any Principals of such Tenant, is a Prohibited Person.

Text Redacted by a third party and not known to Registrant



**EMPLOYMENT AND BENEFITS REPORT**

FOR THE FISCAL YEAR JULY 1, 20[ • ] TO JUNE 30, 20[ • ]  
(THE "REPORTING YEAR")

In order to comply with State and Local Law reporting requirements, the Company is required to complete and return this form to NYCIDA, 110 William Street, Attention: Compliance, New York, NY 10038 no later than the next August 1 following the Reporting Year. PLEASE SEE ATTACHED INSTRUCTIONS AND DEFINITIONS OF CAPITALIZED TERMS USED ON THIS PAGE.

Please provide your NAICS Code (see \_\_\_\_\_)

If you cannot determine your NAICS Code, please indicate industry type: \_\_\_\_\_

- 1. Number of permanent Full-Time Employees as of June 30 of the Reporting Year \_\_\_\_\_
- 2. Number of non-permanent Full-Time Employees as of June 30 of the Reporting Year \_\_\_\_\_
- 3. Number of permanent Part-Time Employees as of June 30 of the Reporting Year \_\_\_\_\_
- 4. Number of non-permanent Part-Time Employees as of June 30 of the Reporting Year \_\_\_\_\_
- 5. Number of Contract Employees as of June 30 of the Reporting Year \_\_\_\_\_
- 6. Total Number of employees of the Company and Its Affiliates included in items 1, 2, 3 and 4 \_\_\_\_\_

Please attach the NYS-45 Quarterly Combined Withholding, Wage Reporting and Unemployment Insurance Return for the period including June 30 of the Reporting Year.

- 7. Number of employees included in item 6 above who reside in the City of New York \_\_\_\_\_
- 8. Do the Company and its Affiliates offer health benefits to all Full-Time Employees? Y N (please circle Y or N)  
Do the Company and its Affiliates offer health benefits to all Part-Time Employees? Y N (please circle Y or N)

If the answer to item 6 above is 250 or more employees, please complete items 9 through 13 below.

- 9. Number of Employees in item 6 who are "Exempt" \_\_\_\_\_
- 10. Number of Employees in item 6 who are "Non-Exempt" \_\_\_\_\_

- |     |   |  |  |
|-----|---|--|--|
| 11. | Number of Employees in item 10 that earn up to \$25,000 annually      |  |  |
| 12. | Number of Employees in item 10 that earn \$25,001 - \$40,000 annually |  |  |
| 13. | Number of Employees in item 10 that earn \$40,001 - \$60,000 annually |  |  |

4 through 13 indicate the value of the benefits realized at Project Locations during the Reporting Period.

- |     |   |                                 |    |
|-----|---|---------------------------------|----|
| 14. | Value of sales and use tax exemption benefits   |                                 | \$ |
| 15. | Value of Commercial Expansion Program ("CEP") benefits  |                                 | \$ |
| 16. | Value of Relocation and Employment Assistance Program ("REAP") benefits   |                                 | \$ |
| 17. | Were physical improvements made to any Project Location during the Reporting Year at a cost exceeding 10% of the current, assessed value of the existing improvements at such Project Location? | Y      N (please circle Y or N) | \$ |

If the Company and/or its Affiliates have applied for Industrial and Commercial Incentive Program ("ICIP") benefits for new physical improvements at Project Location(s), please provide the ICIP application number(s).

**Certification: I, the undersigned, an authorized officer or principal owner of the Company/Affiliate/Tenant, hereby certify to the best of my knowledge and belief, that all information contained in this report is true and complete. This form and information provided pursuant hereto may be disclosed the New York City Economic Development Corporation ("NYCEDC") and New York City Industrial Development Agency ("NYCIDA") and may be disclosed by NYCEDC and NYCIDA in connection with the administration of the programs of NYCEDC and/or NYCIDA and/or the City of New York; and, without limiting the foregoing, such information may be included in (x) reports prepared by NYCEDC pursuant to New York City Charter Section 1301 et. seq., (y) other reports required of NYCIDA or NYCEDC, and (z) any other reports or disclosure required by law.**

Entity Name:		
Signature By:		Date: <span style="border-bottom: 1px solid black;"></span>
Name (print):		Title: <span style="border-bottom: 1px solid black;"></span>

## DEFINITIONS:

“Affiliates” is (i) a business entity in which more than fifty percent is owned by, or is subject to a power or right of control of, or is managed by, an entity which is a party to a Project Agreement, or (ii) a business entity that owns more than fifty percent of an entity which is a party to a Project Agreement or that exercises a power or right of control of such entity.

“Company” includes any entity that is a party to a Project Agreement.

“Contract Employee” is a person who is an independent contractor (i.e., a person who is not an “employee”), or is employed by an independent contractor (an entity other than the Company, an Affiliate or a Tenant), who provides services at a Project Location.

“Financial Assistance” is any of the following forms of financial assistance provided by or at the direction of NYCIDA and/or NYCEDC: a loan, grant, tax benefit and/or energy benefit pursuant to the Business Incentive Rates (BIR) program or New York City Public Utility Service (NYCPUS) program.

“Full-Time Employee” is an employee who works at least 35 hours per week at a Project Location.

“Part-Time Employee” is an employee who works less than 35 hours per week at a Project Location.

“Project Agreement” is any agreement or instrument, pursuant to which an entity received or receives Financial Assistance.

“Project Location” is any location (a) with regard to which Financial Assistance has been provided to the Company and/or its Affiliates during the fiscal year reporting period covered by the Employment and Benefits Report, or (b) that is occupied by the Company and/or its Affiliates at which such entities have employees who are eligible to be reported per the terms of the Project Agreement with the Company and/or its Affiliates.

“Tenant” is a tenant or subtenant (excluding the Company and its Affiliates) that leases or subleases facilities from the Company or its Affiliates (or from tenants or subtenants of the Company or its Affiliates) at any Project Location.

ITEM INSTRUCTIONS For each Project Agreement, please submit one report that covers (i) the Company and its Affiliates and (ii) Tenants and subtenants at all Project Locations covered by this Project Agreement. Each Tenant must complete items 1-5, 15 and 16 on this form with regard to itself and its subtenants and return it to the Company. The Company must include in its report information collected by the Company from its Affiliates and Tenants. The Company must retain for six (6) years all forms completed by its Affiliates and Tenants and at NYCIDA’s request must permit NYCIDA upon reasonable notice to inspect such forms and provide NYCIDA with a copy of such forms. The Company must submit to NYCIDA copies of this form completed by each Tenant.

1-4. Items 1, 2, 3 and 4 must be determined as of June 30 of the Reporting Year and must include all permanent and non-permanent Full-Time Employees and Part-Time Employees at all

Project Locations, including, without limitation, those employed by the Company or its Affiliates and by Tenants and subtenants of Tenants at the Project Locations. Do not include Contract Employees in items 1, 2, 3 and 4.

5. Report all Contract Employees providing services to the Company and its Affiliates and Tenants and subtenants of Tenants at all Project Locations.

6-14. Report information requested only with respect to the Company and its Affiliates at all Project Locations. For item 6, report only the permanent and non-permanent Full-Time Employees and Part-Time Employees of the Company and its Affiliates. Do not report employees of Tenants and subtenants of Tenants. Do not report Contract Employees.

9. Indicated the number of employees included in item 6 who are classified as "Exempt", as defined in the federal Fair Labor Standards Act. Generally, an Exempt employee is not eligible for overtime compensation.

10. Indicate the number of employees included in item 6 who are classified as "Non-Exempt", as defined in the federal Fair Labor Standards Act. Generally, a Non-Exempt employee is eligible for overtime compensation.

14. Report all sales and use tax exemption benefits realized at all Project Locations by the Company and its Affiliates and granted by virtue of the exemption authority of NYCIDA or the City of New York. Do not include any sales and use tax savings realized under the NYS Empire Zone Program.

15. Report all CEP benefits received by the Company and its Affiliates and any Tenants and subtenants of Tenants at all Project Locations. CEP is a package of tax benefits designed to help qualified businesses to relocate or expand in designated relocation areas in New York City. For more information regarding CEP, please visit <http://www.nyc.gov/dof>.

16. Report all REAP benefits received by the Company and its Affiliates and any Tenants and subtenants of Tenants at all Project Locations. REAP is designed to encourage qualified businesses to relocate employees to targeted areas within New York City. REAP provides business income tax credits based on the number of qualified jobs connected to the relocation of employees. For more information regarding REAP, please visit <http://www.nyc.gov/dof>.

LEASE AGREEMENT

Dated as of December 1, 2006

by and between

NEW YORK CITY INDUSTRIAL DEVELOPMENT AGENCY

and

ARE-EAST RIVER SCIENCE PARK, LLC

(ARE-East River Science Park, LLC Project)

Affecting certain Land within the  
Bellevue Hospital Center Campus designated as  
Block 962, Lot 99

in New York County  
City and State of New York  
as more particularly described in  
Exhibit A to this Lease Agreement  
on the Official Tax Map of New York County

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Record and Return to:  
Nixon Peabody LLP  
437 Madison Avenue  
New York, New York 10022  
Attention: Scott R. Singer, Esq.

or both, would constitute an Event of Default hereunder existing or specifying each such default or breach of which such Authorized Representative has knowledge.

(c) The Lessee shall immediately notify the Agency of the occurrence of any Event of Default, or any event that with notice and/or lapse of time would constitute an Event of Default under any Project Document. Any notice required to be given pursuant to this subsection shall be signed by an Authorized Representative of the Lessee and set forth a description of the default and the steps, if any, being taken to cure said default. If no steps have been taken, the Lessee shall state this fact on the notice.

Section 6.9 Employment Information, Opportunities and Guidelines. (a) The Lessee agrees to submit to the Agency on August 1st of each year a completed Employment and Benefits Report in the form of Schedule B – “Employment and Benefits Report” attached hereto to the extent that the Lessee shall have received Financial Assistance (as such term is defined in the Employment and Benefits Report) from the Agency during the twelve-month period ending on the June 30th immediately preceding such August 1st. In addition, upon termination of this Agreement, the Lessee shall submit to the Agency an employment report with respect to both the Lessee and, where so stated, the Tenants, substantially in the form of Schedule B hereto, certified as to accuracy by an Authorized Representative of the Lessee, and shall attach thereto a copy of the Lessee’s final payroll report evidencing the total number of employees employed by the Lessee during the most recent period commencing July 1 of the previous year and ending June 30 of the year of the obligation of filing such report. Annually, by July 31 of each year, commencing on July 1, 2007, until the termination of this Agreement, the Lessee shall submit to the Agency the contact and location report substantially in the form attached hereto as Schedule C.

(b) The Lessee shall ensure that all employees and applicants for employment with the Lessee with regard to the Facility are afforded equal employment opportunities without discrimination. Except as is otherwise provided by collective bargaining contracts or agreements, new employment opportunities created at the Lessee as a result of the Project shall be listed with the New York State Department of Labor Community Services Division, and with the administrative entity of the service delivery area created by the Workforce Investment Act of 1998 (P.L. No. 105-220) in which the Facility is located. Except as is otherwise provided by collective bargaining contracts or agreements, the Lessee agrees, where practicable, to consider first, and cause each of its Affiliates at the Facility to consider first, persons eligible to participate in the Workforce Investment Act of 1998 (P.L. No. 105-220) programs who shall be referred by administrative entities of service delivery areas created pursuant to such act or by the Community Services Division of the New York State Department of Labor for such new employment opportunities.

(c) The Lessee hereby authorizes any private or governmental entity, including but not limited to The New York State Department of Labor (“DOL”), to release to the Agency and/or the New York City Economic Development Corporation (“EDC”), and/or to the successors and assigns of either (collectively, the “Information Recipients”), any and all employment information under its control and pertinent to the Lessee and the employees of the Lessee to enable the Agency and/or EDC to comply with its reporting requirements required by New York City Local Law 48 of 2005 and any other applicable laws, rules or regulations. In addition, upon the Agency’s written request, the Lessee shall provide to the Agency any employment information in

the possession of the Lessee which is pertinent to the Lessee and the employees of the Lessee to enable the Agency and/or EDC to comply with its reporting requirements required by New York City Local Law 48 of 2005 and any other applicable laws, rules or regulations. Information released or provided to Information Recipients by DOL, or by any other governmental entity, or by any private entity, or by the Lessee, or any information previously released as provided by all or any of the foregoing parties (collectively, "Employment Information") may be disclosed by the Information Recipients in connection with the administration of the programs of the Agency, and/or EDC, and/or the successors and assigns of either, and/or The City of New York, and/or as may be necessary to comply with law; and, without limiting the foregoing, the Employment Information may be included in (x) reports prepared by the Information Recipients pursuant to New York City Local Law 48 of 2005, (y) other reports required of the Agency, and (z) any other reports required by law. This authorization shall remain in effect throughout the term of this Agreement.

(d) Nothing in this Section shall be construed to require the Lessee to violate any existing collective bargaining agreement with respect to hiring new employees.

(e) Additionally, the Lessee shall submit to the Agency, together with Schedule B referred to above, a letter of representation that there are no existing tenants at the Project other than the Lessee and tenants authorized pursuant to this Agreement and the Ground Lease.

Section 6.10 Further Assurances. The Lessee will do, execute, acknowledge and deliver or cause to be done, executed, acknowledged and delivered such further acts, instruments, conveyances, transfers and assurances, including Uniform Commercial Code financing statements, at the sole cost and expense of the Lessee, as the Agency deems necessary or advisable for the implementation, effectuation, correction, confirmation or perfection of this Agreement and any rights of the Agency hereunder.

Section 6.11 Recording and Filing. A memorandum of this Agreement, shall be recorded by the Lessee in the appropriate office of the Register of The City of New York, or in such other office as may at the time be provided by law as the proper place for the recordation thereof.

Section 6.12 Further Encumbrances. The Lessee shall not create, permit or suffer to exist any mortgage, encumbrance, lien, security interest, claim or charge against the Facility or any part thereof, or the interest of the Lessee in the Facility or this Agreement or the IDA Lease, except for Permitted Encumbrances.

Section 6.13 Subtenant Survey. The Lessee shall file with the Agency by January 1 and July 1 of each year, commencing January 1, 2007, a certificate of an Authorized Representative of the Lessee with respect to all subtenancies in effect at the Facility, in the form attached hereto as Schedule D.

Section 6.14 Covenants with respect to the Ground Lease.

(a) The Lessee covenants and agrees that it shall not enter into an amendment, supplement or modification to the Ground Lease that would materially and adversely affect the interests of the Agency under the Project Documents without the prior written consent of the Agency.

(b) The Lessee agrees to observe and comply with all of its payments and all of its material obligations, covenants and agreements set forth in the Ground Lease and further agrees to promptly transmit to the Agency copies of any termination or default notice it shall receive from, or deliver to, the City, HHC and/or EDC under the Ground Lease.

(c) The Lessee covenants and agrees that, subject to the provisions of Sections 6.1 and 9.3(a) hereof, it shall remain the tenant under the Ground Lease throughout the term of this Agreement.

Section 6.15 Reporting as to Prohibited Persons. The Lessee shall file with the Agency by August 1 of each year, commencing August 1, 2007, a certification, in the form set forth as Schedule E-1 hereto, that (i) the Lessee is not a Prohibited Person, (ii) the Lessee does not control a Prohibited Person, (iii) none of the members or Principals of any members of the Lessee is a Prohibited Person, and (iv) none of the Principals of the Lessee or any entity or Person which controls the Lessee or the Principals of the Lessee is a Prohibited Person. The Lessee shall attach to such certification the certification, in the form attached hereto as Schedule E-2, delivered to the Lessee from every Major Tenant pursuant to Section 9.3(c)(ii) hereof.

Section 6.16 Environmental Remediation. The Lessee covenants and agrees to comply with Article 21 of the Ground Lease with respect to environmental remediation, and agrees to provide copies of all reports, remediation plans and notices provided, given or received by the Lessee to or from the City pursuant to the Ground Lease or the New York City Department of Environmental Protection.

## ARTICLE VII

### EVENTS OF DEFAULT; REMEDIES

Section 7.1 Events of Default. Any one or more of the following events shall constitute an "Event of Default" hereunder:

(a) Failure of the Lessee to pay when due any Rental Payment and such failure shall continue for a period of ten (10) Business days after notice thereof from Agency to Lessee;

(b) (i) Failure of the Lessee to observe and perform any covenant, condition or agreement on its part to be performed under Sections 2.4, 4.3, 4.4, 4.6, 4.7, 5.1, 6.1, 6.2, 6.3, 6.12, 6.13, 6.14, 7.6, 8.5, 9.3 or 9.14 hereof and continuance of such failure for a period of thirty (30) days after receipt by the Lessee of written notice specifying the nature of such default from the Agency or such longer period as may be required so long as Lessee is diligently prosecuting cure to completion; or

(ii) Failure of the Lessee to observe and perform any covenant or agreement on its part to be performed under Section 4.5 hereof and continuance of such failure for a period



amount of \$500.00 per day until the Lessee shall have recorded the termination of lease with respect to the Facility and terminated this Agreement in accordance with the provisions hereof.

Section 8.5 Recapture of Agency Benefits. It is understood and agreed by the parties to this Agreement that the Agency is entering into this Agreement in order to provide financial assistance to the Lessee for the Project and to accomplish the public purposes of the Act. In consideration therefor, the Lessee hereby agrees as follows:

(a) If there shall occur a Recapture Event after the earlier to occur of (i) the receipt by the Lessee of a temporary certificate of occupancy with respect to the Second Building of the Facility or (ii) the execution and delivery by the Lessee and the Agency of the Mortgage (the "Recapture Commencement Date"), the Lessee shall pay to the Agency as a return of public benefits conferred by the Agency, the following amounts:

(A) one hundred percent (100%) of the Benefits (as defined below) if the Recapture Event occurs within the first (6) years after the Recapture Commencement Date;

(B) eighty percent (80%) of the Benefits if the Recapture Event occurs during the seventh (7th) year after the Recapture Commencement Date;

(C) sixty percent (60%) of the Benefits if the Recapture Event occurs during the eighth (8th) year after the Recapture Commencement Date;

(D) forty percent (40%) of the Benefits if the Recapture Event occurs during the ninth (9th) year after the Recapture Commencement Date; or

(E) twenty percent (20%) of the Benefits if the Recapture Event occurs during the tenth (10th) year after the Recapture Commencement Date.

The term "Benefits" shall mean any exemption from any applicable mortgage recording tax.

The term "Recapture Event" shall mean any of the following events:

(1) The Lessee or the Company shall have liquidated its operations and/or assets (absent a showing of extreme hardship);

(2) The Lessee shall have ceased all or substantially all of its operations at the Buildings (whether by relocation to another facility or otherwise, within or outside of the City) except in connection with a transfer to a Permitted Transferee in accordance with Section 9.3 hereof;

(3) The Lessee shall have terminated this Agreement in accordance with Section 8.1 hereof or the Agency shall have terminated this Lease in accordance with Section 7.2 hereof;

or manufacturing plant or for the purpose of advertising or promoting materials which depict elected or appointed government officials in either print or electronic media, nor shall any funds of the Agency be given hereunder to any group or organization which is attempting to prevent the establishment of an industrial or manufacturing plant within the State.

(k) This Agreement and the other Project Documents constitute the legal, valid and binding obligations of the Lessee enforceable against the Lessee in accordance with their respective terms.

(l) The Lessee is in compliance, and will continue to comply, with all Federal, State and local laws or ordinances (including rules and regulations) relating to zoning, building, safety and environmental quality applicable to the Project and the operation of the Facility.

(m) The Project Cost Budget attached as Exhibit B to this Agreement is true, correct and complete in all material respects, representing as of the Commencement Date, the Lessee's anticipated costs to construct the Project.

(n) Except as permitted by Section 9.3 hereof and the Ground Lease, no Person other than the Lessee is or will be in use, occupancy or possession of any portion of the Project.

(o) The Project will be designed, and the operation of the Facility will be, in compliance with all applicable Federal, State and local laws or ordinances (including rules and regulations) relating to safety and environmental quality.

(p) The Lessee hereby represents that: (i) the Lessee and the Company are not Prohibited Persons, (ii) the Lessee or the Company do not control a Prohibited Person, (iii) none of the members or Principals of any members of the Lessee is a Prohibited Person, and (iv) none of the Principals of the Lessee or the Company or any entity or Person which controls the Lessee or the Company or the Principals of the Lessee or the Company is a Prohibited Person.

(q) The rentable square footage of the Improvements constituting the Project portion of the Facility is anticipated to be approximately 716,000 rentable square feet.

(r) The aggregate acreage of the Land is approximately 2.8 acres.

(s) The fiscal year of the Lessee is the 365 or 366 day period, as the case may be, commencing on January 1, and ending on December 31 of each calendar year.

## ARTICLE II

### CONVEYANCE TO THE AGENCY; THE PROJECT; AND TITLE INSURANCE

Section 2.1 The IDA Lease. Pursuant to the IDA Lease, the Company has subleased the Facility as in existence on the Commencement Date to the Agency, free and clear of all Liens, claims, charges, encumbrances, security interests and servitudes other than Permitted Encumbrances.

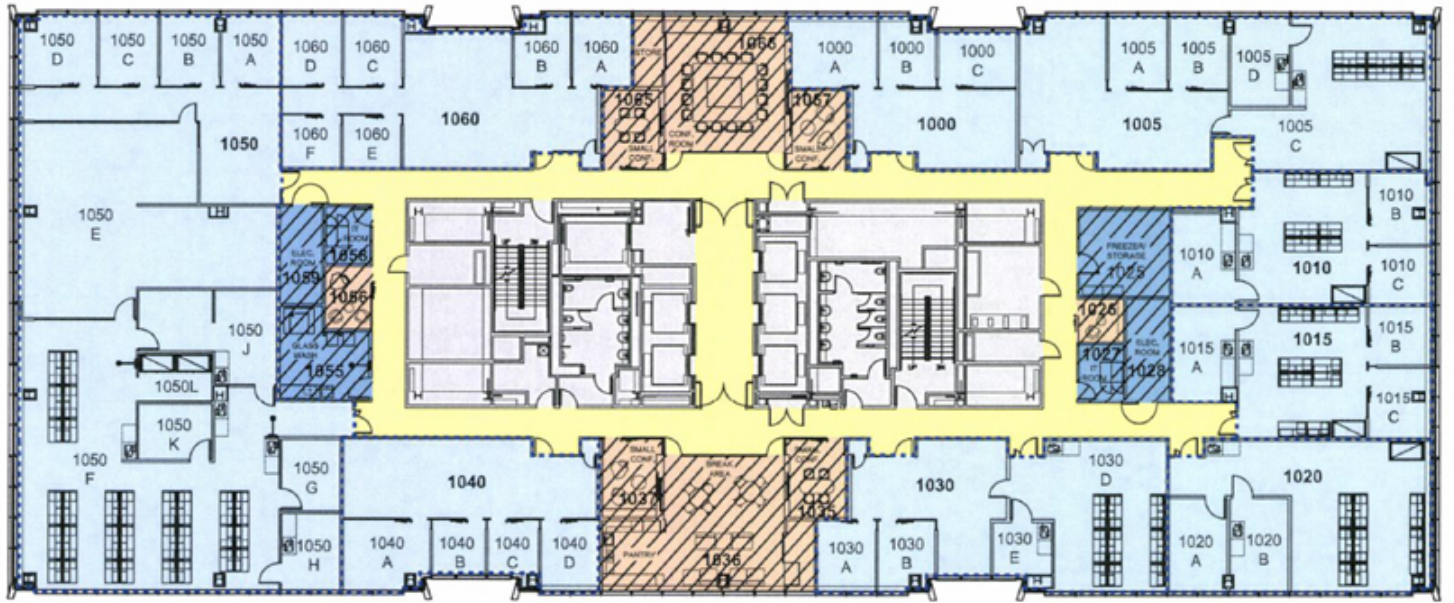
Section 2.2 The Project.

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**EXHIBIT N TO LEASE**

**SHARED LAB AREA**

[See Attached]



## FIRST AMENDMENT TO LEASE

This **FIRST AMENDMENT TO LEASE** (this “**First Amendment**”) is made as of this 3 day of January, 2017, by and between **ARE-EAST RIVER SCIENCE PARK, LLC**, a Delaware limited liability company (“**Landlord**”), and MeiraGTx, LLC, a Delaware limited liability company (“**Tenant**”).

### RECITALS:

**WHEREAS**, Landlord and Tenant have entered into that certain Lease Agreement dated as of June 29, 2016 (the “**Existing Lease**”), whereby Landlord leases to Tenant approximately 5,342 rentable square feet in Suites 1020 and 1030 on the tenth (10<sup>th</sup>) floor of the Building (as defined in the Existing Lease) located at 430 East 29th Street, New York, New York 10016 (the “**Premises**”);

**WHEREAS**, Landlord and Tenant have entered into that certain Lease Agreement dated as of December 15, 2016 (the “**14<sup>th</sup> Floor Lease**”), whereby Landlord leases to Tenant approximately 15,517 rentable square feet on the fourteenth (14<sup>th</sup>) floor of the Building located at 430 East 29th Street, New York, New York 10016 (the “**14<sup>th</sup> Floor Premises**”); and that certain Project Management Agreement dated as of December 15, 2016 (the “**14<sup>th</sup> Floor Project Management Agreement**”); the 14<sup>th</sup> Floor Project Management Agreement, together with the 14<sup>th</sup> Floor Lease, collectively, the “**14<sup>th</sup> Floor Agreements**”), whereby Tenant engaged Landlord to supervise and manage the design and construction of certain improvements in the 14<sup>th</sup> Floor Premises to be constructed pursuant to the Work Letter attached to the 14<sup>th</sup> Floor Lease;

**WHEREAS**, the 14<sup>th</sup> Floor Premises have not yet been issued a temporary certificate of occupancy (the “**14<sup>th</sup> Floor TCO**”); and

**WHEREAS**, Landlord and Tenant desire to amend the Existing Lease on the terms and conditions set forth in this First Amendment.

**NOW, THEREFORE**, in consideration of the foregoing, and for other good and valuable consideration, the receipt and adequacy of which are hereby conclusively acknowledged, the parties hereto agree as follows:

1. **Definitions**. Each capitalized term used herein but not defined herein shall have the respective meaning ascribed to such term in the Existing Lease. From and after the date hereof, all references to the “**Lease**” shall mean the Existing Lease, as modified by this First Amendment.
2. **Amendment to the Lease**. The following shall be added as a new subsection (d) to Section 2 of the Existing Lease:

(d) **Option to Terminate**. Tenant shall have the one-time right to terminate this Lease (the “**Termination Option**”) upon receipt of the 14<sup>th</sup> Floor TCO (the “**TCO Date**”), such termination to become effective on the final day of the month that is ninety (90) days after the Termination Notice Date (as defined below) (the “**Termination Date**”), provided that (i) Landlord receives written notice of Tenant’s election to terminate this Lease (the

“**Termination Notice**”) on or before thirty (30) days after the TCO Date (time being of the essence) (the “**Termination Notice Date**”), (ii) no Default shall exist under this Lease or the 14<sup>th</sup> Floor Agreements, or would exist but for the pendency of any cure period provided for in Section 20 herein, Section 20 of the 14<sup>th</sup> Floor Lease, or Section 7 of the 14<sup>th</sup> Floor Project Management Agreement, as applicable, as of the Termination Notice Date or as of the TCO Date, and (iii) Tenant shall pay to Landlord, with the Termination Notice, a termination fee (the “**Termination Fee**”) in an amount equal to the sum of all unamortized brokerage commissions, and unamortized Base Rent Abatement incurred by Landlord in connection with this Lease. Failure by Tenant to timely pay the Termination Fee shall render any exercise of the Termination Option void and of no further effect. In the event that Tenant has not fulfilled any of the conditions to the exercise by Tenant of the Termination Option or to the Termination Option being valid and effective, Tenant’s right to terminate this Lease, and any purported exercise of the Termination Option, shall lapse and shall be void and of no further force and effect. In such event, any sums which Tenant has paid to Landlord on account of the Termination Fee shall be applied by Landlord to the Base Rent and Additional Rents which thereafter shall become due under this Lease, less any costs incurred by Landlord in connection with Tenant’s attempt to exercise the Termination Option. In addition to the Termination Fee, Tenant shall be obligated to pay all Rent due to and through the Termination Date and shall surrender the Premises to Landlord on or before the Termination Date in the manner and in the condition as herein provided. Tenant shall permit Landlord or Landlord’s Related Parties (as hereinafter defined), at any time upon reasonable notice, to enter the Premises, without charge therefore to Landlord and without diminution of Rent, to exhibit the same to prospective tenants after the Termination Notice Date. The Termination Fee shall not be deemed to be Rent payable under the terms of the Lease, but rather shall be deemed liquidated damages payable by Tenant to Landlord in consideration of Landlord’s agreement to terminate the Lease as herein provided. Upon termination in accordance with this Section 2(d), neither party shall have any obligations to the other under this Lease except for those obligations that survive expiration or earlier termination of this Lease as expressly set forth in this Lease. Notwithstanding a termination of this Lease in accordance with this Section 2(d), the 14<sup>th</sup> Floor Agreements shall remain unmodified and in full force and effect.

3. **Miscellaneous**

- (a) Except as specifically modified in this First Amendment, all covenants, terms and conditions contained in the Lease remain unmodified and in full force and effect and are hereby ratified and confirmed in all respects. The Lease, as amended by this First Amendment, constitutes the entire understanding between the parties hereto with respect to the Premises and supersedes any prior or contemporaneous written or oral statements, agreements or representations made by either party or any of its representatives. Each party represents and warrants to the other party hereto that it has no knowledge of any default by the other party under the Lease through the date of the execution of this First Amendment.
- (b) If any clause or provision of this First Amendment is illegal, invalid or unenforceable under present or future laws, then and in that event, it is the intention of the parties hereto that the remainder of this First Amendment shall not be affected thereby.

- (c) This First Amendment shall be binding on and inure to the benefit of the successors and permitted assigns of the respective parties.
- (d) Landlord and Tenant each represent and warrant that it has not dealt with any broker, agent or other person (collectively, "**Broker**") in connection with this transaction, and that no Broker brought about this transaction. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by virtue of having dealt with Tenant or Landlord, as applicable, with regard to this leasing transaction.
- (e) This First Amendment shall be governed by and construed in accordance with the internal laws of the State of New York applicable to agreements made and to be performed entirely within New York, without regard to conflict of laws principles, and shall be resolved in a proceeding within the State of New York.
- (f) This First Amendment may be signed in counterparts, each of which shall be deemed an original and all of which together shall constitute one and the same instrument.
- (g) The Lease may not be modified, amended, changed or terminated orally, but only by an agreement in writing signed by the party against whom enforcement of the modification, amendment, change or termination is sought.
- (h) Tenant represents and warrants that (i) the Lease is in full force and effect and has not been modified except as expressly set forth in this First Amendment, (ii) to Tenant's actual knowledge, neither Landlord nor Tenant is in default of any of its respective obligations under the Lease, and no event has occurred that, with the passage of time and/or the giving of notice would constitute a default by either Landlord or Tenant thereunder, and (iii) all Base Rent and Additional are paid in full through the date hereof, and as of the date hereof, Tenant claims no offsets, setoffs, rebates, concessions or defenses against or with respect to the payment of Base Rent, Additional Rent or any other sums payable by Tenant under the Lease.

[SIGNATURES APPEAR ON THE FOLLOWING PAGE]

IN WITNESS WHEREOF, the parties have caused their duly authorized representatives to execute this First Amendment as of the date first written above.

**LANDLORD:**

**ARE-EAST RIVER SCIENCE PARK, LLC,**  
a Delaware limited liability company

By: **ALEXANDRIA REAL ESTATE  
EQUITIES, L.P.**, a Delaware limited  
partnership,  
managing member

By: **ARE-QRS CORP.**,  
a Maryland corporation,  
general partner

By: /s/ Gary Dean  
Name: Gary Dean  
Title: Senior Vice President RE  
Legal Affairs

**TENANT:**

**MEIRAGTX, LLC,**  
a Delaware limited liability company

By: /s/ Rich Giroux  
Name: Rich Giroux  
Title: Chief Operating Officer



## SECOND AMENDMENT TO LEASE

This **SECOND AMENDMENT TO LEASE** (this “**Second Amendment**”) is made as of this 4 day of January, 2017, by and between **ARE-EAST RIVER SCIENCE PARK, LLC**, a Delaware limited liability company (“**Landlord**”), and **MEIRAGTX, LLC**, a Delaware limited liability company (“**Tenant**”).

### RECITALS:

**WHEREAS**, Landlord and Tenant have entered into that certain Lease Agreement dated as of June 29, 2016, as amended by that certain First Amendment to Lease, dated as of January 3, 2017 (collectively, the “**Existing Lease**”), whereby Landlord leases to Tenant approximately 5,342 rentable square feet in Suites 1020 and 1030 on the tenth (10<sup>th</sup>) floor (the “**Existing Premises**”), of the Building (as defined in the Existing Lease) located at 430 East 29th Street, New York, New York 10016;

**WHEREAS**, Tenant desires to license from Landlord the 545 square feet of space in Suite 1060-C on the tenth (10<sup>th</sup>) floor of the Building as shown on Exhibit A attached hereto (the “**Office Space**”); and

**WHEREAS**, Landlord and Tenant desire to amend the Existing Lease on the terms and conditions set forth in this Second Amendment.

**NOW, THEREFORE**, in consideration of the foregoing, and for other good and valuable consideration, the receipt and adequacy of which are hereby conclusively acknowledged, the parties hereto agree as follows:

1. **Definitions**. Each capitalized term used herein but not defined herein shall have the respective meaning ascribed to such term in the Existing Lease. From and after the date hereof, all references to the “**Lease**” shall mean the Existing Lease, as modified by this Second Amendment.
2. **License of Office Space**. Landlord hereby licenses to Tenant the Office Space, subject to the terms and conditions hereinafter described (the “**License**”).
3. **Rent**. There shall not be any additional Base Rent payable on account of the License.
4. **Permitted Use**. Tenant shall use the Office Space solely as an office and not for any other purpose. Tenant shall use the Office Space in accordance with all of the applicable terms and conditions of the Existing Lease.
5. **License Term**. The License is effective as of January 1, 2017, and shall terminate on the earlier of June 30, 2017 and the 30<sup>th</sup> day following any written notice of termination delivered by Landlord, which notice of termination may be given at any time in Landlord’s sole discretion. On or before the date of termination of the License, Tenant shall vacate and surrender the Office Space to Landlord vacant and in the same condition as received.

6. **Insurance.** Tenant shall amend all of the existing insurance policies maintained by it pursuant to the provisions of the Existing Lease, or acquire new insurance policies which provide the same coverage as if required to be maintained under the provisions of the Existing Lease, to provide coverage for the Office Space, any activities conducted therein, and any liability of or to any licensee, occupant, invitee or guest in the Office Space, or in the common areas of the Building or the Project, in accordance with the insurance requirements described in Section 17(a) of the Existing Lease.
7. **Indemnification.** Tenant agrees that its obligations to indemnify Landlord under any provision of the Existing Lease shall include, incorporate and extend to, for any and all purposes, the Office Space, any activities conducted therein, and any liability of or to any licensee, occupant, invitee or guest in the Office Space, or in the common areas of the Building or the Project, in accordance with the indemnification provisions set forth in Section 16 of the Existing Lease.
8. **Miscellaneous.**
  - (a) Except as specifically modified in this Second Amendment, all covenants, terms and conditions contained in the Existing Lease remain unmodified and in full force and effect and are hereby ratified and confirmed in all respects. The Existing Lease, as amended by this Second Amendment, constitutes the entire understanding between the parties hereto with respect to the Premises and supersedes any prior or contemporaneous written or oral statements, agreements or representations made by either party or any of its representatives. Each party represents and warrants to the other party hereto that it has no knowledge of any default by the other party under the Lease through the date of the execution of this Second Amendment.
  - (b) If any clause or provision of this Second Amendment is illegal, invalid or unenforceable under present or future laws, then and in that event, it is the intention of the parties hereto that the remainder of this Second Amendment shall not be affected thereby.
  - (c) This Second Amendment shall be binding on and inure to the benefit of the successors and permitted assigns of the respective parties.
  - (d) Landlord and Tenant each represent and warrant that it has not dealt with any broker, agent or other person (collectively, "**Broker**") in connection with this transaction, and that no Broker brought about this transaction. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by virtue of having dealt with Tenant or Landlord, as applicable, with regard to this leasing transaction.
  - (e) This Second Amendment shall be governed by and construed in accordance with the internal laws of the State of New York applicable to agreements made and to be performed entirely within New York, without regard to conflict of laws principles, and shall be resolved in a proceeding within the State of New York.

- (f) This Second Amendment may be signed in counterparts, each of which shall be deemed an original and all of which together shall constitute one and the same instrument.
- (g) The Lease may not be modified, amended, changed or terminated orally, but only by an agreement in writing signed by the party against whom enforcement of the modification, amendment, change or termination is sought.
- (h) Tenant represents and warrants that (i) the Existing Lease is in full force and effect and has not been modified except as expressly set forth in this Second Amendment, (ii) to Tenant's actual knowledge, neither Landlord nor Tenant is in default of any of its respective obligations under the Lease, and no event has occurred that, with the passage of time and/or the giving of notice would constitute a default by either Landlord or Tenant thereunder, and (iii) all Base Rent and Additional Rent are paid in full through the date hereof, and as of the date hereof, Tenant claims no offsets, setoffs, rebates, concessions or defenses against or with respect to the payment of Base Rent, Additional Rent or any other sums payable by Tenant under the Lease.

[SIGNATURES APPEAR ON THE FOLLOWING PAGE]



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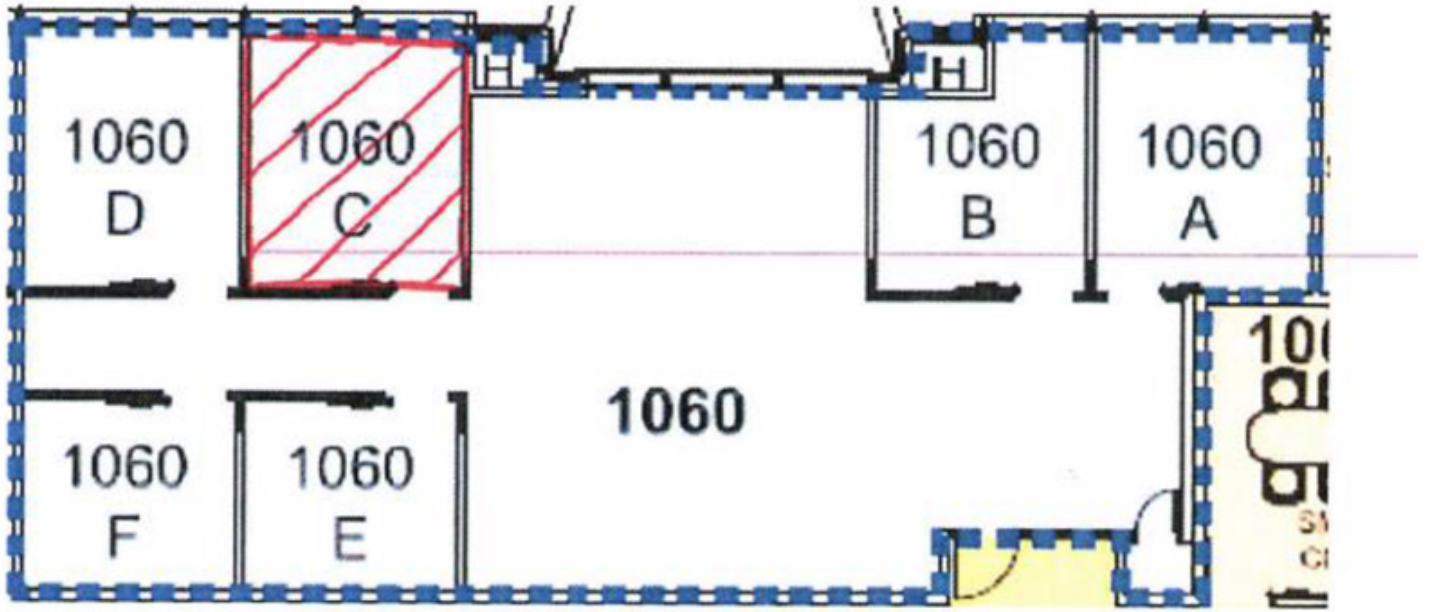
**EXHIBIT A**

**DESCRIPTION OF OFFICE SPACE**

[See Attached]

Exhibit A

Description of Suite 1060-C Premises



Dated

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**MOORFIELDS EYE HOSPITAL NHS FOUNDATION TRUST**

**and**

**MEIRAGTX LIMITED**

**and**

**KADMON CORPORATION LLC**

---

**UNDERLEASE  
of Pharmacy Manufacturing Unit  
34 Nile Street  
London N1**

---

© Bevan Brittan LLP

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T 0370 194 1000 F 0370 194 1001

Fleet Place House 2 Fleet Place Holborn Viaduct London EC4M 7RF  
T 0370 194 1000 F 0370 194 7800

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T 0370 194 1000 F 0370 194 5001

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## PARTICULARS

**DATE:**

**Landlord:** **MOORFIELDS EYE HOSPITAL NATIONAL HEALTH SERVICE FOUNDATION TRUST** of City Road London EC1V 2PD

**Tenant:** **MEIRAGTX LIMITED** incorporated and registered in England and Wales with company number 09501998 whose registered office is c/o Legalinx Limited, 1 Fetter Lane, London EC4A 1BR

**Guarantor:** **KADMON CORPORATION LLC** a limited liability company formed under the laws of the State of Delaware, USA whose head office is at 450 East 29<sup>th</sup> Street, 16<sup>th</sup> Floor, New York, NY 10016, United States of America and whose address for service in England is The Pharmacy Manufacturing Unit, 34 Nile Street, London N1 (or such other address in England as may be notified by the Guarantor to the Landlord in writing from time to time)

**Premises:** The pharmacy manufacturing unit comprising part of the ground floor of Block E, the basement and sub-basement levels, the Fresh Air Inlet, the fire escape forming part of Block B and the Service Tower as shown edged red on Plans 3 to 10 attached to the Superior Lease and as more specifically defined in Clause 1.2 of this Lease

**Contractual Term:** 5 years from and including the Term Commencement Date

**Term Commencement Date:** the date of this Lease

**Rent Commencement Date:** the date of this Lease

**Rent:** two hundred and fifteen thousand six hundred pounds (£215,600) per annum

**Permitted Use:** as a pharmacy manufacturing unit with ancillary offices, loading and storage space or any other use subject to the Landlord's and Superior Landlord's consent

**Service Charge:** the Service Charge payable by the Landlord pursuant to the Superior Lease

**THIS LEASE** is made as a deed on the date and between the parties specified in the Particulars

## **1. INTERPRETATION**

### **1.1 Particulars**

In this Lease the words and expressions contained in the Particulars have the meanings specified in the Particulars but as further defined (if applicable) in Clause 1.2 and elsewhere in this Lease.

### **1.2 Definitions**

In this Lease (unless the context otherwise requires) the following words and expressions have the following meanings:

**1954 Act** means the Landlord and Tenant Act 1954;

**1995 Act** means the Landlord and Tenant (Covenants) Act 1995;

**Act of Insolvency** means any of the following:

- (a) the taking of any step in connection with any voluntary arrangement or any other compromise or arrangement for the benefit of any creditors of the Tenant or any guarantor;
- (b) the making of an application for an administration order or the making of an administration order in relation to the Tenant or any guarantor;
- (c) the giving of any notice of intention to appoint an administrator, or the filing at court of the prescribed documents in connection with the appointment of an administrator, or the appointment of an administrator, in any case in relation to the Tenant or any guarantor;
- (d) the appointment of a receiver or manager or an administrative receiver in relation to any property or income of the Tenant or any guarantor;
- (e) the commencement of a voluntary winding-up in respect of the Tenant or any guarantor, except a winding-up for the purpose of amalgamation or reconstruction of a solvent company in respect of which a statutory declaration of solvency has been filed with the Registrar of Companies;
- (f) the making of a petition for a winding-up order or a winding-up order in respect of the Tenant or any guarantor;
- (g) the striking-off of the Tenant or any guarantor from the Register of Companies or the making of an application for the Tenant or any guarantor to be struck-off;
- (h) the Tenant or any guarantor otherwise ceasing to exist (but excluding where the Tenant or any guarantor dies); or
- (i) the presentation of a petition for a bankruptcy order or the making of a bankruptcy order against the Tenant or any guarantor.

The paragraphs above shall apply in relation to a partnership or limited partnership (as defined in the Partnership Act 1890 and the Limited Partnerships Act 1907 respectively) subject to the modifications referred to in the Insolvent Partnerships Order 1994 (*SI 1994/2421*) (as amended) and a

limited liability partnership (as defined in the Limited Liability Partnerships Act 2000) subject to the modifications referred to in the Limited Liability Partnerships Regulations 2001 (*SI 2001/1090*) (as amended).

Act of Insolvency includes any analogous proceedings or events that may be taken pursuant to the legislation of another jurisdiction in relation to a tenant or guarantor incorporated or domiciled in such relevant jurisdiction.

**Authorised Guarantee Agreement** means an authorised guarantee agreement as defined in section 16 of the 1995 Act;

**Authorised Guarantor** means any person who enters into an Authorised Guarantee Agreement pursuant to this Lease;

**Block E** means the ground to fifth floor building shown for identification only shaded yellow on Plan 2 attached to the Superior Lease but which for the avoidance of doubt excludes the Service Tower;

**Common Parts** means those parts of the Superior Landlord's Estate which are designated by the Superior Landlord in its reasonable discretion for use and capable of use by the Tenant in common with the Superior Landlord and all other tenants and occupiers and those authorised by them shown for the purpose of identification only edged green and hatched green on Plan 2 attached to the Superior Lease (including (without limitation) the Courtyard) and the area of paving beside Block E shown edged and hatched brown on Plan 5 attached to the Superior Lease and the Conduits (other than those Conduits exclusively serving the Premises);

**Completion Date** means the date determined in accordance with clause 14.10.

**Conduits** means sewers drains gutters ducts pipes wires cables watercourses high pressure water mains and other conducting media and also manholes inspection chambers tanks pumps transformer substations and apparatus used in conjunction with them;

**Courtyard** means the internal courtyard shown edged green on Plan 2 attached to the Superior Lease;

**CRC Scheme** means the carbon trading scheme established by the CRC Energy Efficiency Scheme Order 2010, and includes any similar scheme that replaces or supplements it;

**Estimated Service Charge** as defined in the Superior Lease;

**Fresh Air Inlet** means the fresh air inlet exclusively serving the Premises shown edged red on Plan 2 attached to the Superior Lease including any part or parts above ground level in the Courtyard.

**Group Company** means a company that is a member of the same group within the meaning of section 42 of the 1954 Act;

**Guarantor** means a person who guarantees any or all of the Tenant's Obligations in this Lease including an Authorised Guarantor and including any personal representative of them;

**Insurance Rent** means the sum payable by the Landlord to the Superior Landlord pursuant to clause 5 of the Superior Lease.

**Insured Risks** means fire, storm, tempest, lightning, explosion, earthquake, (fire and shock) aircraft and articles falling from them except in times of war, riot, civil commotion, malicious damage, impact by road vehicles, flood, burst and overflow of water pipes tanks or apparatus and such other risks as the Superior Landlord may insure against from time to time (subject in each case to such exclusions limitations conditions and excesses as the Superior Landlord from time to time reasonably agrees with the Insurers) but excluding any risk against which the Superior Landlord does not insure because cover is not ordinarily available in the London insurance market or is only available in that market subject to conditions or at a premium which the Superior Landlord considers unacceptable;

**Insurers** means the insurers from time to time of the Premises;

**Interest** means interest at the Interest Rate (both before and after judgment) accruing on a daily basis and compounded with quarterly rests on the Quarter Days;

**Interest Rate** means 3% above the base lending rate from time to time of Lloyds TSB plc or such other bank (being a member of the Committee of London and Scottish Bankers) as the Landlord may from time to time nominate in writing or (if base lending rates of banks forming such Committee cease to be published or the Committee ceases to exist) such other comparable rate of interest as the Landlord reasonably specifies;

**Landlord's Expenses** means solicitors' counsels' surveyors' and other consultants' and professionals' fees and costs bailiffs' fees including all disbursements;

**Landlord's Financial Year** means 1 April in any year to 31 March in the year following or such other period of twelve months as the Superior Landlord may from time to time decide provided that the last financial year shall determine upon termination of this Lease;

**Landlord's Conveyancer** means Bevan Brittan LLP of Fleet Place House, 2 Fleet Place, Holborn Viaduct, London EC4M 7RF, (Reference: 63863.154/Ian Caplan) or any other conveyancer whose details may be notified in writing from time to time by the Landlord to the Tenant;

**Landlord's Representative** means the Landlord's Surveyor or any other appropriately qualified person the Landlord from time to time appoints to represent it with regard to this Lease;

**Law** means Act of Parliament, statutory instrument, regulation, bye-law, requirement of a competent authority, statutory body, utility company or authority, common law or regulation, directive or mandatory requirement of the European Union;

**this Lease** means this lease as varied from time to time together with any document which is supplemental to or collateral with or entered into pursuant to it;

**Liability** means all actions proceedings costs claims demands losses expenses and liabilities;

**Loading Bay** means the loading bay shown hatched orange and shaded green on Plan 5 attached to the Superior Lease;

**New Lease:** the lease of the Property (the terms of which are set out in Clause 14.5) to be granted upon the exercise of the Option;

**Normal Business Hours** means 8.00 am to 7.00 pm Mondays to Fridays and 8.00 am to 1.00 pm on Saturdays (excluding all public holidays);

**Option** means the option granted by the Landlord to the Tenant by Clause 14;

**Option Notice** means written notice exercising the Option in accordance with Clause 14;

**Option Period** means the period from and including the date of this lease up to and including the last day of the fourth year of the Contractual Term;

**Outgoings** means all present and future rates taxes duties charges assessments impositions and outgoings (whether or not of a capital or nonrecurring nature and including any of a novel nature);

**Plans** means the plans 1 – 10 annexed to the Superior Lease;

**Premises** means the Premises as defined in the Particulars including:

- (a) the interior fascias of all walls and columns in the lower basement and upper basement and the lower basement floor slab and the upper basement floor/ceiling slab and the ceiling slab forming the roof of the basement (including the part forming the floor of the Courtyard) and of the room at upper and lower basement levels housing the cavity drainage pump and the waste water sump pump referred to in (i) below and of the fire escape stairwell at upper and lower a basement level (but not at ground floor level) forming part of Block B (the upper and lower basement being shown edged red on Plans 3 and 4 attached to the Superior Lease); and
- (b) the interior fascias of all walls columns and the floor and ceiling slabs of Block E at ground floor level (the ground floor level being edged red on Plan 5 attached to the Superior Lease); and
- (c) the interior fascias of all walls columns of and the floor and ceiling slabs of the Service Tower; and
- (d) the interior fascia of the roof of the flammable waste store at first floor level of the Service Tower; and
- (e) all fixtures and fittings from time to time; and
- (f) any carpets and blinds provided by the Landlord; and
- (g) all improvements alterations and additions to the Premises and

- (h) all Conduits which are within or (to the extent within the Landlord's Estate and which have not been publicly adopted) exclusively serve the Premises; and
- (i) all plant and machinery within or exclusively serving the Premises including without limitation lifts central heating lighting air conditioning fresh air venting systems and the cavity drainage pump under Block B and the waste water sump pump under Block B and the fire alarm and sprinkler systems; and
- (j) all doors windows glass door and window furniture; and
- (k) raised floors; and
- (l) suspended ceilings their means of attachment and voids above them; and
- (m) the hoist lift shaft from the lower basement to the first floor of the Service Tower and the stairwell from the lower basement level to ground level shown at ground level shaded yellow and purple respectively on Plan 5 attached to the Superior Lease; and
- (n) the Loading Bay and the air space above it from ground to second floor level; and
- (o) all internal non-structural walls and partitioning  
and any reference to the Premises includes any part of them (except where the word is used in Clause 3.11 and 3.12)

**President** means the president of the RICS or any person authorised to act on his behalf;

**Quarter Days** means 25<sup>th</sup> March, 24<sup>th</sup> June, 29<sup>th</sup> September and 25<sup>th</sup> December in each calendar year and "Quarter Day" means any one of them;

**Rents** means all sums made payable by Clause 2;

**Review Date** means the first day of the term of the New Lease;

**RICS** means the Royal Institution of Chartered Surveyors or any institution association or other body of which (by reason of amalgamation or otherwise and whether or not retaining a separate identity) the RICS may become a constituent part or which may replace it;

**Service Tower** means the service tower adjacent to Block E at the ground to fifth floors shown edged red on Plans 5 and 6 attached to the Superior Lease and shown edged green on Plans 7-10 attached to the Superior Lease;

**Structure** means the structure comprises:

- (a) the structural framework structural floors structural walls and external walls of all floor levels and the foundations and roof of Block E including the canopy of the Loading Bay but excluding the Service Tower; and

- (b) the structural framework and structural walls and floor and external cavity wall abutting the stairwell on the southern elevation of the Courtyard and the flank walls comprising a single skin of blockwork and the cladding of the stairwell walls of the Service Tower including the ventilation louvres and the roof of the flammable waste store at first floor level of the Service Tower; and
- (c) any structural parts of the lower basement and upper basement shown respectively with red edging on Plans 3 and 4 attached to the Superior Lease including the lower basement floor slab, the upper basement floor slab and roof slab forming the roof of the basement immediately below ground level including internal supporting columns and the block and concrete wall enclosure below ground including for the avoidance of doubt the party wall with the Landlord's Car Park; and
- (d) the Conduits, which serve the Premises jointly with other premises; and
- (e) any plant and machinery serving the Premises jointly with other premises; and
- (f) the structural parts of the Fresh Air inlet and including the louvres in the flank wall;

but excluding the Premises;

**Superior Landlord** means the landlord for the time being of the Superior Lease;

**Superior Landlord's Car Park** means the car park at basement level immediately adjacent to the Premises at basement level and the access ramp;

**Superior Landlord's Covenants** means the obligations in the Superior Lease to be observed by the Superior Landlord;

**Superior Landlord's Estate** means the freehold land at Nile Street Britannia Walk Ebenezer Street and Vestry Street in the London Borough of Hackney shown edged blue on Plan 1 attached to the Superior Lease and registered at the Land Registry under title number EGL249920;

**Superior Landlord's Surveyor** means any suitably qualified person from time to time appointed by the Landlord to carry out surveying and/or management functions relating to the Premises;

**Superior Lease** means the lease by virtue of which the Landlord holds the Property, which is dated 12 October 2001 and made between (1) Islington and Shoreditch Housing Association Limited and (2) Moorfields Eye Hospital NHS Trust and any documents made supplemental to it;

**Superior Rent** means the annual rent payable by the Landlord under clause 2.1 of the Superior Lease;

**Tenant's Default** means a breach by the Tenant of covenant warranty or obligation in this Lease;

**Tenant's Obligation** means a covenant or obligation of a tenant;

**Term** means the Contractual Term and any period of continuation holding over or extension of it;

**Third Party Rights** means all the matters referred to in Schedule 1 of this Lease;

**Utilities** means any of foul and surface water drainage air water gas steam electricity communication and other similar services and supplies;

**VAT** means Value Added Tax or any tax or duty of a similar nature substituted for or in addition to it.

1.3

### **Miscellaneous**

In this Lease:

- 1.3.1 **“Landlord”** includes any person from time to time entitled to the immediate reversion to this Lease;
- 1.3.2 **“Tenant”** includes the Tenant’s successors in title and assigns and (if an individual) his personal representative;
- 1.3.3 **“Guarantor”** includes (if an individual) his personal representative;
- 1.3.4 a reference to an Act of Parliament includes all derivative instruments orders regulations and other matters and in each case any re-enactment amendment consolidation or modification from time to time of that Act and any derivative instruments orders regulations or other matters (except in the case of a reference to the Town & Country Planning (Use Classes) Order 1987 and the reference to the Value Added Tax Act 1994 in Clause 3.19.2 which shall be read as amended as at 1 August 2000);
- 1.3.5 an obligation owed by more than one person is owed by them jointly and severally;
- 1.3.6 a reference to the Tenant or a Guarantor includes a reference to each person comprising them;
- 1.3.7 an obligation by the Tenant or the Landlord not to do something includes an obligation not to permit or allow it to be done;
- 1.3.8 a reference to an act or omission of the Tenant includes an act or omission of any undertenant and any other person deriving title under the Tenant and includes an act or omission of their respective employees and visitors and anyone at the Premises with the express or implied authority of any one or more of them;
- 1.3.9 a reference to a Clause or to a Schedule is a reference to a Clause or Schedule of this Lease and a reference to a paragraph is a reference to a paragraph of the relevant Schedule of this Lease;
- 1.3.10 any area or thing shown or marked on the Plans shall be shown or marked for the purpose of identification only;
- 1.3.11 a reference to the end of the Term is to the end of the Term however it determines;
- 1.3.12 a consent or approval of the Landlord or the Tenant to be valid must be in writing;



- 1.3.13 references to any consent or approval required from the Landlord shall be construed as also including a requirement to obtain the consent or approval of the Superior Landlord, where such consent or approval is required under the terms of the Superior Lease except that nothing in this lease shall be construed as imposing on the Superior Landlord any obligation (or indicating that such an obligation is imposed on the Superior Landlord by the terms of the Superior Lease) not unreasonably to refuse any such consent;
- 1.3.14 any notice given to the Landlord to be valid must be in writing and must (unless the Landlord specifies otherwise) be given before the event or action to which it relates;
- 1.3.15 where the Landlord is not lawfully entitled unreasonably to withhold any licence consent approval or acknowledgement required under the terms of this Lease the Landlord shall not unreasonably withhold or delay the issue of the same nor proffer the same subject to unreasonable conditions;
- 1.3.16 a right of the Landlord to have access to or entry upon the Premises extends to any superior landlord and any mortgagee of the Building and to anyone properly authorised by the Landlord or any superior landlord or mortgagee and includes a right of entry with workmen equipment and materials;
- 1.3.17 a right of the Tenant to have access or entry upon any part of the Landlord's Estate extends to any lawful undertenant or occupier of the Premises and to anyone properly authorised by the Tenant or such undertenant or occupier and includes a right of entry with workmen equipment and materials;
- 1.3.18 the table of contents and headings to Clauses, paragraphs and Schedules do not affect the construction of this Lease;
- 1.3.19 a right granted by the Landlord is granted in common with all other persons entitled to it and/or authorised by the Landlord to exercise it;
- 1.3.20 a right excepted or reserved to the Landlord is also reserved to any other person entitled to it and/or properly authorised by the Landlord;
- 1.3.21 where the Landlord is entitled to enter the Premises (whether by virtue of a covenant by the Tenant or rights reserved) it shall only do so on reasonable written notice to the Tenant save where access is required immediately in the event of an emergency in which case the Landlord on giving notice, may break and enter if it reasonably considers it necessary;
- 1.3.22 nothing entitles the Tenant to enforce any obligation given by anyone to the Landlord;
- 1.3.23 any works (whether of repair, decoration, alteration or otherwise) that the Landlord or Tenant is permitted or obliged to carry out in accordance with this Lease must be carried out with good quality materials and to a reasonable standard and in accordance with good modern practice;
- 1.3.24 a Landlord's Representative may be an employee of the Landlord or a Group Company of the Landlord;
- 1.3.25 any payment or other consideration to be provided by one party to the other is exclusive of VAT;
- 1.3.26 any termination of this Lease is without prejudice to any then accrued claims of any party against any other;

- 1.3.27 a provision of this Lease which is void or unenforceable shall be severed from all other provisions of this Lease and the remaining provisions shall continue to have effect;
- 1.3.28 if a provision of this Lease extends beyond the limitations set by any Law or rule of law but if it were not so extended would remain unaffected by the Law or rule of law, the provision is deemed to be varied so as not to extend beyond the limitations;
- 1.3.29 if any matter is referred to arbitration pursuant to this Lease:
- (a) it is to be conducted in accordance with the Arbitration Act 1996; and
  - (b) the arbitrator has no power to order a rectification of this Lease or direct that the recoverable costs of the arbitration or any parts of the arbitral proceedings will be limited to a specific amount;
- 1.3.30 if any matter in this Lease is to be determined by an expert or an arbitrator:
- (a) he is to be appointed by agreement between the Landlord and the Tenant or at the request and option of either of them is to be nominated by the President;
  - (b) if he dies, delays or declines to act, the President may on the application of either the Landlord or the Tenant discharge him and appoint another to act in his place in the same capacity; and
  - (c) if either the Landlord or the Tenant pays his fees and expenses, it may recover the proportion (if any) the other party was obliged to pay from that other party as a debt recoverable on demand;
- 1.3.31 “assign” includes “transfer”;
- 1.3.32 “decorate” includes paint paper and otherwise treat as appropriate and applies to all areas usually or previously painted papered or treated and any requirement to paint is a requirement to paint with at least two coats of good quality paint and “decoration” is interpreted in a similar manner;
- 1.3.33 any reference to a “fair proportion” is to a fair and reasonable proportion as reasonably and properly determined by the Landlord or a Landlord’s Representative;
- 1.3.34 “include” “includes” and “Including” are deemed to be followed by the words “without limitation”;
- 1.3.35 “on demand” means within 5 days of written demand;
- 1.3.36 general words introduced by “other” do not have a restrictive meaning;
- 1.3.37 “sign” includes notice, display, flagpole, hoarding, aerial, satellite dish and advertisement (whether illuminated or not).
- 1.3.38 Notwithstanding anything to the contrary in this Lease the Tenant (so long as it is a Health Service Body) shall not be obliged to pay the Rents or any other payment due under this Lease unless it has received a proper invoice for the relevant rent or payment at least 30 days beforehand and any such rent or payment shall be deemed not to be due under this Lease until 30 days after receipt by the Tenant of such invoice.
- 1.3.39 Where a circumstance or condition is stated to be determined by the Landlord or by any other person then the power to determine is to be exercised reasonably and properly unless otherwise stated;

## **2. DEMISE**

2.1 The Landlord with full title guarantee demises the Premises to the Tenant for the Contractual Term together with (but to the exclusion of all other rights) the rights set out in Schedule 1 of the Superior Lease except and reserving to the Landlord and the Superior Landlord the rights set out in Schedule 2 of the Superior Lease subject to the Third Party Rights yielding and paying to the Landlord by way of rent:

- 2.1.1 the Rent by four equal instalments in advance on or before the Quarter Days;
- 2.1.2 the Insurance Rent payable on demand;
- 2.1.3 the Service Charge payable at the times and in the manner specified in Clause 3.3;
- 2.1.4 any VAT payable by the Tenant in accordance with Clause 3.19;
- 2.1.5 any sums payable in accordance with Clause 3.21

## **3. TENANT'S COVENANTS**

The Tenant covenants with the Landlord as follows:

### **3.1 Rents**

To pay the Rents in accordance with Clause 2;

### **3.2 Outgoings and Utilities**

- 3.2.1 Promptly to pay all Outgoings at any time charged or assessed on or in respect of the Premises and in the absence of any direct assessment to pay to the Landlord on demand a fair proportion of them;
- 3.2.2 The obligation in Clause 3.2.1 excludes any taxes payable by the Landlord (other than VAT) on receipt of Rents or which arise from a dealing with the Landlord's interest in the Premises or any other payment which the Landlord as the person entitled to the reversion on determination of this Lease is bound by law to pay;
- 3.2.3 If the Landlord or Superior Landlord loses rating relief at any time because it has been allowed to the Tenant or anyone else to make good the loss to the Landlord or the Superior Landlord (as appropriate) on demand;
- 3.2.4 To pay the suppliers for and indemnify the Landlord and the Superior Landlord (as the case may be) against all charges for Utilities supplied to the Premises and to pay all equipment rents for equipment which exclusively serve the Premises;
- 3.2.5 To comply with the requirements and regulations of any company or authority supplying Utilities to the Premises;
- 3.2.6 To pay the whole or (if applicable) a fair proportion of the costs and expenses incurred by the Landlord (or, if relevant, any other person who is registered under the CRC Scheme as being responsible for the Landlord) in connection with its participation in the CRC Scheme.

### **3.3 Service Charge**

- 3.3.1 The Landlord will notify the Tenant before or during any Service Charge Period of the Estimated Service Charge payable by the Tenant during that Service Charge Period.

- 3.3.2 The Tenant shall pay on account of the Service Charge for each Landlord's Financial Year the Estimated Service Charge by four equal quarterly instalments on the Quarter Days PROVIDED that in the event the Landlord's Financial Year shall not comprise a full calendar year the Landlord shall make such adjustments to the foregoing arrangements as are reasonably required in order to ensure that the Tenant shall not pay more than the Estimated Service Charge in respect of the relevant Landlord's Financial Year.
- 3.3.3 The Landlord shall on receipt from the Superior Landlord serve on the Tenant a notice containing a summary of the Superior Landlord's expenses and outgoings and a statement of the amount of the Service Charge for such year.
- 3.3.4 An amount equal to the difference between the Service Charge for the relevant Landlord's Financial Year and all payments made on account of the Service Charge by the Tenant for that year shall be paid by the Tenant to the Landlord within seven days of the service of the notice referred to in Clause 3.3.3 or allowed by the Landlord to the Tenant against the payment or payments on account of the Service Charge due from the Tenant next following the service of such notice.
- 3.3.5 Any omission by the Superior Landlord to include in any summary of the Superior Landlord's said expenses and outgoings for any Landlord's Financial Year or in the statement of the amount of the Service Charge for any such year a sum expended or a liability incurred in that year shall not preclude the Superior Landlord from including such sums or the amount of such liability in any subsequent Landlord's Financial Year.
- 3.3.6 If at any time during the Landlord's Financial Year the Superior Landlord shall reasonably consider it necessary to incur any expenses in complying with the obligations of the Landlord contained in Clause 4 of the Superior Lease or in respect of the other matters mentioned in Schedule 2 of the Superior Lease for which no adequate provision shall have been made in calculating the payments on account of the Service Charge the Landlord may require the Tenant at any time to pay to the Landlord within fourteen days the Service Charge Contribution of the amount of the deficit.

#### 3.4 **Repair**

- 3.4.1 To keep such part or parts of the Premises in good and substantial repair and condition as are not the Superior Landlord's obligation to repair and maintain pursuant to Clause 4 of the Superior Lease including for the avoidance of doubt the cavity drainage pump and the waste water sump pump under Block B;
- 3.4.2 The obligation in Clause 3.4.1 includes an obligation to renew and rebuild when necessary;
- 3.4.3 Subject to Clause 3.8.11 to replace and renew any Landlord's fixtures and fittings (including carpets and other floor-coverings) and/or Superior Landlord's fixtures and fittings in or forming part of the Premises which are or become missing broken damaged stained or destroyed and which are not the Superior Landlord's obligation to repair and maintain pursuant to Clause 4 of the Superior Lease with new ones of equivalent quality to the reasonable satisfaction of the Landlord and/or the Superior Landlord;
- 3.4.4 Damage by Insured Risks is excepted from the obligations in this Clause 3.4 save to the extent that any insurance money is irrecoverable by reason of a Tenant's Default and the Tenant has not paid such unrecoverable monies to the Landlord;

3.5

**Decoration and Upkeep**

- 3.5.1 In the last six months before the end of the Term to decorate the exterior of those parts of the Premises which are above ground and which are normally decorated; and which are not the Superior Landlord's obligation to repair and maintain pursuant to Clause 4 of the Superior Lease;
- 3.5.2 All decoration must be in such colours and with such materials as the Landlord and/or Superior Landlord may reasonably require;
- 3.5.3 To keep the Premises clean and tidy;
- 3.5.4 To clean the inside and outside of the windows of the Premises when required;
- 3.5.5 To replace immediately all broken or damaged glass in or forming part of the Premises with glass of similar tint and specification;
- 3.5.6 To cause all gas electric hydraulic and other mechanical installations and equipment forming part of the Premises to be used and maintained in a reasonable manner;
- 3.5.7 To carry out all works of repair and cleaning of the Premises in a reasonable manner;

3.6

**Yield Up**

- 3.6.1 By the end of the Term (and subject to Clause 3.8.11):
  - (a) to remove from the Premises all signs (other than those installed by or on behalf of the Landlord and/or the Superior Landlord) and all tenant's fixtures and fittings furniture and effects and to make good to the reasonable satisfaction of the Landlord and the Superior Landlord all damage caused by the removal;
  - (b) unless otherwise required by the Landlord and/or Superior Landlord in writing, to re-instate and restore the Premises to their state and condition prior to the carrying out of any works or alterations to the Premises during the Term;
  - (c) to hand over to the Landlord any health and safety files and maintenance records relating to the Premises;
- 3.6.2 At the end of the Term to yield up the Premises to the Landlord with vacant possession and in compliance with all the Tenant's Obligations in this Lease;

3.7

**Rights of Entry and to Ensure Repair**

- 3.7.1 To permit the Landlord and/or Superior Landlord to enter the Premises to carry out its obligations under this Lease and to exercise any rights excepted and reserved in this Lease and/or the Superior Lease;
- 3.7.2 To commence all works which are a Tenant's Obligation in this Lease within one month (or sooner if necessary) after service of notice by the Landlord and/or Superior Landlord requiring them to be carried out and to complete the works and to remedy any Tenant's Default specified in a notice given by the Landlord and/or Superior Landlord as quickly as reasonably practicable;
- 3.7.3 If the Tenant does not complete such works and remedy any specified Tenants Default within a reasonable period after service of such notice to permit the Landlord (without prejudice to its rights of re-entry contained in this Lease) and/or Superior Landlord to enter the Premises to carry out any uncompleted works and to do anything to remedy

the Tenant's Default and the Tenant will reimburse the Landlord or Superior Landlord (as the case may be) on demand the cost of doing so (including all Landlord's Expenses);

- 3.7.4 To give immediate written notice to the Landlord on becoming aware of any defects in the Premises which may give rise to a liability or duty on the Landlord and/or Superior Landlord under any Law and to allow the Landlord and/or Superior Landlord to display any notice on the Premises it may require in relation to those defects;

### 3.8 Alterations

- 3.8.1 Not to make any alterations or additions to the Premises unless allowed by the following parts of this Clause 3.8;
- 3.8.2 The Tenant may install and remove non-structural, demountable partitioning without the consent of the Landlord provided that the Tenant makes good any damage caused to the Premises by such installation and removal;
- 3.8.3 Not to make any structural alterations or additions to the Premises or to make any changes to the external appearance of the Premises without the Landlord's prior written consent (which shall not be unreasonably withheld or delayed) and the Superior Landlord's consent in accordance with the terms of the Superior Lease.
- 3.8.4 Not to make any internal non-structural alteration to the Premises without the Landlord's prior written consent (which shall not be unreasonably withheld or delayed);
- 3.8.5 Not to carry out any alteration or addition which hinders reasonable access to a Conduit or a fire exit PROVIDED that where reasonable to do so the Tenant may reroute any Conduit provided that reasonable access to such Conduit and fire exit is maintained;
- 3.8.6 To supply to the Landlord and the Superior Landlord all plans and specifications the Landlord and/or the Superior Landlord may reasonably require to identify any proposed works and to carry out all works only in accordance with such approved plans and specifications and to the reasonable satisfaction of the Landlord and the Superior Landlord;
- 3.8.7 After commencing any permitted works of alteration to complete them by the earliest of:
- (a) a date which is a reasonable period after they have been commenced;
  - (b) the end of the Term;
- 3.8.8 Any consent for alterations may be on such conditions and on such terms as the Landlord and/or the Superior Landlord may reasonably require;
- 3.8.9 Not to carry out any alteration except by a reputable contractor;
- 3.8.10 Not to alter any electrical wiring in the Premises except in accordance with the recommendations of the Institute of Electrical Engineers or any other appropriate body reasonably specified by the Landlord and/or the Superior Landlord;
- 3.8.11 The Tenant shall remove any alterations or additions or works to the Premises carried out during the Term or prior to commencement of the Term by or on behalf of the Tenant (including for the avoidance of doubt such works or parts as may have become part of the Premises or the Landlord's fixtures and fittings or the Superior Landlord's fixtures and fittings) and shall make good to the reasonable satisfaction of the Landlord and the Superior Landlord all damage caused by their removal;

3.8.12 Not to affix any additions fixtures or fittings or plant or machinery to or make any alterations to or which might adversely affect the Structure without first obtaining the Landlord's prior written consent (such consent not to be unreasonably withheld or delayed) and the consent of the Superior Landlord.

3.9 **Signs**

3.9.1 Not to exhibit or erect any sign which is visible from outside the Premises;

3.9.2 To permit the Landlord and/or the Superior Landlord to fix and retain upon any part of the outside of the Premises (but so as not to obscure the windows thereof or interfere with the Tenant's use thereof) a sign (during the last six months of the Term) for the reletting of the Premises and (at any time) for the sale of the Premises and to permit the Landlord and/or the Superior Landlord to show the Premises to prospective tenants, mortgagees and purchasers or their agents at reasonable times by prior appointment;

3.9.3 Not to erect a sign identifying the name of the building forming Block E of which the Premises forms part other than with a name selected and designated by the Landlord and the Superior Landlord.

3.10 **Use**

3.10.1 Not to use the Premises other than for the Permitted Use;

3.10.2 To ensure at all times the safe handling and storage of chemicals radioactive and other like materials

3.10.3 Not to do anything which causes a nuisance annoyance disturbance or inconvenience loss or damage to the Landlord and/or the Superior Landlord or any other person PROVIDED that the use of the Premises for the Permitted Use in a reasonable manner so as not to cause an unlawful nuisance to the Landlord and/or the Superior Landlord or other tenants and occupiers of the Superior Landlord's Estate shall not be a breach of this covenant PROVIDED FURTHER that if any complaint is made by the Landlord and/or the Superior Landlord or any other tenant of the Superior Landlord's Estate the Tenant will investigate such complaint and if substantiated and it is reasonable to do so will diligently and expeditiously take all reasonable steps to rectify, mitigate and resolve the source of the complaint

3.10.4 Not to leave the Premises unoccupied for more than one month without first giving notice to the Landlord and the Superior Landlord;

3.10.5 Not knowingly to allow any encroachment or new easement to be made on or against the Premises;

3.10.6 Not to give any acknowledgement that an easement or right benefiting the Premises is enjoyed by consent or otherwise;

3.10.7 Not to stop-up darken or obstruct any window light or way belonging to the Premises;

3.10.8 To give immediate notice to the Landlord and the Superior Landlord on becoming aware of:

- (a) an encroachment on or circumstance which might result in the acquisition of an easement or other right over the Premises; or

- (b) the obstruction of a right of which the Premises has the benefit; and to take or join in such proceedings or take such other steps as the Landlord may reasonably require in connection with the same at the cost of the Landlord;

3.10.9 To observe and perform the regulations set out in Clause 3.22.

### 3.11 Underletting

3.11.1 In this Clause 3.11 the following words and expressions have the following meanings:

- (a) **“Permitted Underlease”**: an underlease of the whole of the Premises which fulfils all of the following criteria:
  - (i) its yearly rent is not less than the open market rental value (without taking a fine or premium or other valuable consideration) reasonably obtainable for the premises underlet at the time of the grant and subject to rent review to the open market rental value at intervals of not more than five years;
  - (ii) its rent is not commuted or payable for more than one quarter in advance;
  - (iii) no fine or premium is reserved or taken;
  - (iv) it contains covenants by the undertenant:
    - (a) not to assign or charge any part of the premises underlet as distinct from the whole;
    - (b) not to sub-underlet any part of the premises underlet nor part with or share the occupation of the whole or any part of the premises underlet except by way of an assignment or charge of the whole;
    - (c) not to assign or charge the whole of the premises underlet without first obtaining the Landlord’s consent (which is not to be unreasonably withheld) and the Superior Landlord’s consent; and
    - (d) otherwise consistent with the Tenant’s Obligations in this Lease;
  - (v) its form is approved by the Landlord and the Superior Landlord prior to its grant (but the approval will not be unreasonably withheld);

3.11.2 The Tenant will not part with or share possession or occupation of the whole or any part or parts of the Premises unless allowed by this Clause 3.11;

3.11.3 The Tenant will not hold the whole or any part of the Premises on trust for another;

3.11.4 The Tenant may underlet the whole of the Premises only:

- (a) by a Permitted Underlease; and
- (b) with the Landlord’s consent (which will not be unreasonably withheld or delayed); and, of the Superior Landlord in accordance with the terms of the Superior Lease and



- (c) provided that if the Landlord so requires the undertenant first executes a deed (in such form as the Landlord and/or the Superior Landlord may reasonably require) containing a direct covenant with the Landlord and the Superior Landlord to perform and observe the obligations on the part of the tenant in the Underlease and any document that is supplemental or collateral to it and the tenant covenants in this Lease, except the covenants to pay the rents reserved by this Lease;

3.11.5 For the purposes of the Landlord's consent in Clause 3.11.4(b), it is reasonable (but not by way of limitation) for the Landlord to stipulate as a condition of giving that consent that it may be revoked if:

- (a) after the consent but before the grant of the underlease a material to the Tenant which would enable the Landlord to withhold its consent if a fresh application were then made; or
- (b) the underlease is not completed and a certified copy of it given to the Landlord within 2 months of the consent;

3.11.6 Once an underlease is granted the Tenant will:

- (a) not without the prior consent of the Landlord and the Superior Landlord vary or waive the terms of or accept any surrender of the Underlease (except for a surrender of the whole with the Landlord's consent which will not be unreasonably withheld or delayed and the Superior Landlord's consent in accordance with the terms of the Superior Lease);
- (b) take all reasonable steps to enforce the obligations of the parties to the underlease including (if the Landlord requires) exercising any right of re-entry;
- (c) not knowingly permit any breach of any Tenant's Obligation in the underlease;

3.11.7 The Tenant will on written request at any time by the Landlord give to the Landlord in writing the full names and addresses of everyone in occupation of the Premises together with the area occupied and a certified copy of all documents permitting the occupation or (if none) a written memorandum of any relevant agreement;

3.11.8 The Tenant will reply to any notice served under section 40 of the 1954 Act by or on behalf of the Landlord within the time prescribed by the 1954 Act;

3.11.9 The Tenant will not unreasonably withhold its consent to any request by the Landlord or any predecessor to be released from its obligations in this Lease after it has transferred its interest in the Premises.

## 3.12 **Assignment**

### 3.12.1 **Assignment**

- (a) The Tenant shall not assign the whole of this Lease without the consent of the Landlord, such consent not to be unreasonably withheld.
- (b) The Tenant shall not assign part only of this Lease.
- (c) The Landlord and the Tenant agree that for the purposes of section 19(1A) of the Landlord and Tenant Act 1927 the Landlord may give its consent to an assignment subject to a condition that the assignor (and any former tenant who because of section 11 of the Landlord and Tenant (Covenants) Act 1995 has

not been released from the tenant covenants of this Lease) enters into an authorised guarantee agreement which:

- (i) is in respect of all the tenant covenants of this Lease;
  - (ii) is in respect of the period beginning with the date the assignee becomes bound by those covenants and ending on the date when the assignee is released from those covenants by virtue of section 5 of the Landlord and Tenant (Covenants) Act 1995;
  - (iii) imposes principal debtor liability on the assignor (and any former tenant);
  - (iv) requires (in the event of a disclaimer of liability under this Lease) the assignor (or former tenant as the case may be) to enter into a new tenancy for a term equal to the unexpired residue of the Contractual Term; and
  - (v) is otherwise in a form reasonably required by the Landlord.
- (d) The Landlord and the Tenant agree that for the purposes of section 19(1A) of the Landlord and Tenant Act 1927 the Landlord may refuse its consent to an assignment if any Rent or other money due under this Lease is outstanding.
- (e) Nothing in this clause 3.12.1 shall prevent the Landlord from giving consent subject to any other reasonable condition, nor from refusing consent to an assignment in any other circumstance where it is reasonable to do so.

### 3.13 **Charging**

3.13.1 The Tenant shall not charge the whole of this Lease without the consent of the Landlord, such consent not to be unreasonably withheld.

3.13.2 The Tenant shall not charge part only of this Lease.

### 3.14 **Registration**

Within one month after any disposition affecting the Premises to send to the Landlord's solicitors a certified copy of the document evidencing it and to pay such registration fee as the Landlord may reasonably require (being not less than £50 plus VAT) in respect of each such document;

### 3.15 **Notices**

Within 7 days (or sooner if necessary) of receipt to produce to the Landlord and the Superior Landlord a certified copy of any notice order permission or proposal given issued or made to or on the Tenant in respect of the Premises by any competent authority pursuant to an Act of Parliament affecting the Premises or their use and at the request of the Landlord and/or the Superior Landlord to make or join with the Landlord and/or the Superior Landlord in making such objections or representations in respect of it as the Landlord and/or the Superior Landlord may reasonably require;

### 3.16 **Laws**

3.16.1 Not to breach any Law that applies to the Premises;

- 3.16.2 To comply with all Laws which at any time affect the Premises anti/or their use and/or the employment of people in them;
- 3.16.3 To supply to the Landlord and the Superior Landlord on reasonable request from time to time a copy of the current fire certificate for the Premises and thereafter any amendments or endorsements thereto.

3.17 **Planning and Environmental**

- 3.17.1 In this Clause 3.17 “Planning Acts” means the Acts of Parliament defined as the “consolidating Acts” in section 1(1) of the Planning (Consequential Provisions) Act 1990 and the Planning and Compensation Act 1991 and any other Laws from time to time in force relating to town and country planning;
- 3.17.2 To comply with the Planning Acts;
- 3.17.3 Not to make any application under the Planning Acts without the Landlord’s consent which shall not be unreasonably withheld or delayed and the consent of the Superior Landlord;
- 3.17.4 To supply the Landlord and the Superior Landlord with a copy of any application made or permission granted under the Planning Acts as soon as it is made with copies of any plans or drawings relating to it and to keep the Landlord and the Superior Landlord informed of the progress of the application and its result;
- 3.17.5 Not to commence any development permitted under the Planning Acts without the Landlord’s consent which shall not be unreasonably withheld or delayed and the consent of the Superior Landlord;
- 3.17.6 Not to enter into any agreement or obligation or serve any purchase notice under the Planning Acts without the Landlord’s consent which shall not be unreasonably withheld or delayed and the consent of the Superior Landlord;
- 3.17.7 If the Landlord and/or the Superior Landlord reasonably so requires, before the end of the Term to complete any works authorised under the Planning Acts which were commenced but not finished by the Tenant or any undertenant or anyone on their behalf;
- 3.17.8 Not to permit any substance which causes or might cause harm to human health or the environment or which affects the Superior Landlord’s Estate or neighbouring property to be brought onto the Premises or to pass through any Conduits in or serving the Premises provided that the use of the Premises for the Permitted Use in a reasonable manner and in accordance with the covenants on the part of the Tenant contained in Clause 3.10.2 and Clause 3.22 shall not be a breach of this covenant.

3.18 **Landlord’s Expenses**

- 3.18.1 To pay to the Landlord on demand all reasonable Landlord’s Expenses reasonably and properly incurred charged or payable by the Landlord and/or the Superior Landlord in connection with the following:
  - (a) an application for consent or approval under this Lease unless such consent licence or approval is unreasonably withheld or is proffered subject to unreasonable conditions;
  - (b) obtaining any necessary superior landlord’s and/or mortgagee’s consent arising from an application by the Tenant;
  - (c) supervising any works carried out by or on behalf of the Tenant;

- 3.18.2 To pay to the Landlord on demand on an indemnity basis all Landlord's Expenses properly incurred charged or payable by the Landlord in connection with or in contemplation of any of the following:
- (a) a notice under sections 146 or 147 of the Law of Property Act 1925 and/or the Leasehold Property (Repairs) Act 1938 and/or any proceedings pursuant to such notice (whether or not forfeiture is avoided otherwise than by relief granted by a competent court);
  - (b) a Tenant's Default;
  - (c) a schedule of dilapidations whenever it is served which relates to failure to repair, decorate, carry out works and/or remove works during or at the end of the Term (provided that no such Schedule shall be prepared more than 6 months after the end of the Term);
  - (d) supervising any works to remedy a Tenant's Default;

3.19 **VAT**

- 3.19.1 To pay any VAT chargeable on any payment or other consideration due under or in connection with this Lease on the later of the date that the payment or other consideration is due and delivery of a valid VAT invoice to the payer;
- 3.19.2 In every case where the Tenant has agreed to pay or indemnify the Landlord against any payment made by the Landlord under the terms of or in connection with this Lease the Tenant will also reimburse any VAT paid by the Landlord on that payment insofar as the same is not recoverable by the Landlord as input tax;
- 3.19.3 In the event that the identity of the Tenant or its use of the Premises shall cause any Landlord's election to waive exemption from VAT in respect of the Premises to be disappplied under paragraph 2 (2) and 2 (3AA) of Schedule 10 of the Value Added Act 1994 to pay to the Landlord on demand any repayment of VAT due and paid to Customs & Excise and any irrecoverable input VAT incurred by the Landlord in respect of the Premises as a result of such disapplication

3.20 **Indemnity**

To indemnify the Landlord against Liability arising directly or indirectly from a Tenant's Default;

3.21 **Interest**

If any Rents or other sums due under this Lease are unpaid for a period of more than 14 days to pay to the Landlord on demand Interest on them from and including the due date until payment;

3.22 **Regulations**

- 3.22.1 Not to deposit any rubbish in the Premises other than in proper receptacles and to ensure that they are regularly emptied;
- 3.22.2 Not to overload the Premises or damage overload or obstruct any Conduits plant machinery or equipment in or serving them;

- 3.22.3 Not to use the Premises for any illegal purpose nor allow anyone to reside or sleep at the Premises or to gamble or bet in them;
- 3.22.4 Not to use the Premises for any noisy offensive or dangerous purpose provided that the use of the Premises for the Permitted Use in a reasonable manner and in accordance with Clause 3.10.2 shall not be a breach of this Clause 3.22.4;
- 3.22.5 Not to hold on the Premises a political meeting public show spectacle or sale by auction;
- 3.22.6 To exercise the rights in Schedule 1 of the Superior Lease strictly in accordance with the provisions of that Schedule;
- 3.22.7 To ensure that the Landlord and the Superior Landlord and the local police have written notice of the name address and home telephone number of at least two keyholders of the Premises;
- 3.22.8 Not to allow in the Premises any machinery or equipment which is not appropriate for the Permitted Use or which causes noise or vibration provided that the use of the Premises for the Permitted Use in a reasonable manner and in accordance with Clause 3.10.2 shall not be a breach of this Clause 3.22.8;
- 3.22.9 Not to play any music in the Premises which can be heard outside them;
- 3.22.10 Not to allow any animals to be in the Premises;
- 3.22.11 To use all lifts in the Premises in accordance with their design capacities and operators' instructions;
- 3.22.12 Without avoidable delay to give notice to the Landlord and the Superior Landlord of any right to be granted by or to the Tenant pursuant to the Telecommunications Act 1984 with full details of any works to be carried out as a result of the grant of that right and (unless approved by the Landlord and the Superior Landlord under any other provision of this Lease) at the cost of the Superior Landlord to withhold any agreement to the right or works for so long as the Tenant is reasonably able to do so or until the Landlord and/or the Superior Landlord otherwise reasonably stipulates;
- 3.22.13 To comply with such reasonable regulations as the Landlord or the Superior Landlord may from time to time prescribe for the conduct and/or management of the Common Parts;
- 3.22.14 Not to park load or unload vehicles except in the Loading Bay and not to load or unload any vehicles other than during Normal Business Hours PROVIDED THAT the Tenant will use all reasonable endeavours to ensure that loading unloading and deliveries take place before 6.00 pm on Mondays to Fridays and not all at the weekends except between the hours of 8.00am - 1.00pm on Saturdays

3.23 **Encumbrances**

To comply with all covenants and other matters affecting the Premises set out in the documents (if any) in Schedule 1.

3.24 **Clinical and other Waste**

To store remove and procure the disposal of all clinical commercial and other waste safely and in accordance with Law;

3.25 **Covenant to comply with covenants in the Superior Lease**

The Tenant shall observe and perform the tenant covenants in the Superior Lease except the covenants to pay the rents reserved by the Superior Lease but in the event of any conflict between the covenants by the Tenant in this Lease and the tenant covenants by the tenant covenants in the superior Lease then the covenants by the tenant in this lease shall prevail.

4. **LANDLORD'S COVENANT**

The Landlord covenants with the Tenant:

4.1 **Quiet Enjoyment**

That, so long as the Tenant pays the rents reserved by and complies with its obligations in this Lease, the Landlord will allow the Tenant peaceably and quietly to use and enjoy the Premises without lawful interference by the Landlord or anyone who derives title from the Landlord or any person lawfully claiming through under or in trust for the Landlord or by title paramount.

4.2 **Superior Lease Rents**

The Landlord shall pay the rents reserved by the Superior Lease.

4.3 **Superior Lease**

At the request and cost of the Tenant, on a full indemnity basis the Landlord shall use all reasonable endeavours to procure that the Superior Landlord complies with the Superior Landlord's covenants during such period as the Superior Lease subsists and, if reasonable, the Landlord may require that the Tenant pay it reasonable security in advance in respect of anticipated costs for enforcing such compliance.

5. **RIGHTS EXCEPTED AND RESERVED**

The following rights are excepted and reserved from this Lease to the Landlord for the benefit of the Landlord:

5.1 **Car Parking Space**

The right at all times to park a motor vehicle in one of the car parking spaces at the Property.

6. **INSURANCE PROVISIONS**

6.1 The Landlord shall use its reasonable endeavours to procure that the Superior Landlord complies with the covenants imposed on it regarding insurance contained in the Superior Lease save to the extent that the policy of insurance has been vitiated or any insurance proceeds withheld in consequence of any act or omission of the Tenant or its workers, contractors or agents or any person on the Premises with the actual or implied authority of any of them. Neither the Superior Landlord nor the Landlord shall be obliged to insure any part of the Premises installed by the Tenant.

6.2 **The Tenant covenants with the Landlord:**

6.2.1 to pay to the Landlord on demand after receipt of adequate details of the insurance for the Premises, the Insurance Rent;

6.2.2 to pay to the Landlord on demand any amount that is deducted or disallowed by the Superior Landlord's insurers pursuant to any excess provision in the insurance policy;

- 6.2.3 if the payment of any insurance monies is refused due to a Tenant's Default to pay on demand to the Landlord or the Superior Landlord the amount refused;
- 6.2.4 not to effect insurance of the Premises against any Insured Risk save to the extent that the Landlord and/or the Superior Landlord shall not have insured the Premises or any part thereof;
- 6.2.5 to apply all monies it receives from any insurance policy for the Premises or items in or attached to the Premises in making good the relevant loss or damage PROVIDED THAT the Tenant shall not be obliged to reinstate any alterations or additions carried out by or on behalf of the Tenant or any person deriving title under it (including for the avoidance of doubt such works or part as may have become part of the Premises);
- 6.2.6 not to cause any policy of insurance relating to the Premises to become void or voidable PROVIDED THAT:
- (a) the Landlord shall request from the Superior Landlord copies or sufficient extracts of the policies of insurance on request by the Tenant and supply to the Tenant copies on receipt from the Superior Landlord; and
  - (b) the Tenant shall supply a copy of its public liability insurance cover in such amount as the Landlord and/or the Superior Landlord shall reasonably require (subject to such insurance being available on reasonable terms in the London insurance market at a reasonable premium and subject to such excesses exclusions and conditions as are required by the insurers) and in the event of any breach of this covenant by the Tenant the same shall be deemed a Tenant's Default;
- 6.2.7 to pay any increased premium for any policy of insurance relating to the Premises arising solely from the Tenant's use of the Premises in accordance with the Permitted Use;
- 6.2.8 to comply with the Insurers' requirements notified to the Tenant and those of any competent authority notified to the Tenant regarding the Premises or use of them;
- 6.2.9 not to allow any dangerous or inflammable materials to be at the Premises provided that the use of the Premises for the Permitted Use in a reasonable manner and in accordance with the covenants on the part of the Tenant contained in Clause 3.10.2 and Clause 3.22 shall not be a breach of this covenant;
- 6.2.10 once it becomes aware to give immediate notice to the Landlord and the Superior Landlord of any event or circumstance which may lead to or affect an insurance claim.
- 6.3 If the Premises are destroyed or so substantially damaged that the Landlord receives notice from the Superior Landlord that it will not be able to substantially rebuild or reinstate for any reason:
- 6.3.1 the Landlord shall forthwith serve notice on the Tenant; and
  - 6.3.2 either party may subsequently determine this Lease by not less than one month's written notice to the other such notice to be served within 12 months of the date of damage or destruction.
- 6.4 If the Premises are destroyed or substantially damaged and shall not have been substantially rebuilt or reinstated by a date three years after the date of damage or destruction either party may within one month after such date serve on the other written notice of determination of this Lease and the Lease shall be determined with immediate effect

6.5 Determination of the Lease pursuant to Clause 6.3 or 6.2 shall be without prejudice to the antecedent rights either party may have against the other.

6.6 This Lease shall terminate immediately prior to termination of the Superior Lease if:

6.6.1 the Superior Landlord serves notice on the Landlord pursuant to clause 5.7 or 5.8 of the Superior Lease; or

6.6.2 the Landlord serves notice on the Superior Landlord pursuant to clause 5.8 of the Superior Lease.

6.7 If the Premises or any part shall be destroyed or damaged by any of the Insured Risks so as to be unfit for occupation or use then save to the extent that the insurance of the Premises shall have been vitiated by any act neglect default or omission of the Tenant or any sub-tenant or their respective servants agents licensees or invitees the rents reserved or a fair and just proportion according to the nature and extent of the damage sustained (the amount of such proportion if it cannot be agreed to be determined by a single arbitrator to be appointed on the application of either party by the President for the time being (or other next senior officer available) of the Royal Institution of Chartered Surveyors whose decision shall be final and binding) shall be suspended until the Premises or the damaged portion shall have been reinstated or made fit for occupation and use.

## 7. PROVISOS

### 7.1 Agreement and Declaration

**PROVIDED THAT AND IT IS AGREED AND DECLARED** as set out in this Clause 7;

### 7.2 Re-Entry

7.2.1 If:

(a) the Rents (other than the Rent) or any other sums payable under this Lease are not paid within 21 days after they become due ; or

(b) a Tenant's Default occurs;

then the Landlord may re-enter the Premises and the Term will then end but without prejudice to any accrued claim of either party against the other;

### 7.3 Warranty concerning Use

The Landlord does not warrant that the Premises may be used for the Permitted Use without breaching any Law.

### 7.4 Superior Landlord's Estate

7.4.1 In this Clause 7.4 "Permitted Person" means the Superior Landlord, any Group Company of the Landlord and anyone authorised by either of them.

7.4.2 A Permitted Person may at any time carry out any works to the Superior Landlord's Estate (excluding the Premises) and/or may use the Superior Landlord's Estate as the Superior Landlord thinks fit in its reasonable discretion and the Permitted Person shall not be liable to the Tenant nor shall the Tenant object or make a claim for disturbance



and inconvenience which results from the carrying out of those works in a reasonable manner or that use so long as any works are completed as soon as reasonably practicable PROVIDED THAT none of the developments alterations and/or rebuilding permitted by this Clause shall adversely affect the Permitted Use of the Premises.

7.4.3 The rights granted in Schedule 1 of the Superior Lease a Permitted Person may develop alter or re-build any part of the Superior Landlord's Estate whether or not this obstructs or interferes with light or air to the Premises PROVIDED THAT no machinery producing noise or vibration shall be placed by the Landlord on the roof of the Premises AND PROVIDED FURTHER THAT none of the developments alterations and/or rebuilding permitted by this Clause shall adversely affect the Permitted Use of the Premises.

7.4.4 The Tenant does not have and shall not acquire any easement right or privilege over the Superior Landlord's Estate except for those (if any) granted in Schedule 1 of the Superior Lease and section 62 of the Law of Property Act 1925 does not apply to this Lease.

## 7.5 Notices

The rules about serving notices in section 196 of the Law of Property Act 1925 (as amended by the Recorded Delivery Service Act 1962) apply to any notice given under this Lease (unless otherwise provided by statute) PROVIDED THAT so long as Moorfields Eye Hospital National Health Service Trust is the Landlord any notice shall be served on it at its address contained in this Lease and marked for the attention of the Chief Executive or at such other address or to such other officer as is notified in writing by the Landlord to the Tenant from time to time.

## 7.6 Understanding and Representations

7.6.1 This Lease embodies the entire understanding of the parties.

7.6.2 The Tenant acknowledges that it has not entered into this Lease relying wholly or partly on any statement or representation made by or on behalf of the Landlord unless the statement:

7.6.3 was not capable of verification by search or enquiry of any statutory body; and

7.6.4 it was made in this Lease or in writing by the Landlord's solicitors to the Tenant's solicitors before its grant.

## 7.7 Suspension of Services

The Landlord and/or the Superior Landlord is entitled to suspend any services or Utilities to the Premises or to stop or divert any Conduits while it carries out inspections or repairs provided that reasonable prior written notice is given to the Tenant and provided further that no such suspension diversion or stopping up which has any material adverse effect on the Premises or any part thereof or on the use or enjoyment of or access to the same shall be effected unless it is unavoidable or avoidable only at a cost which the Landlord and/or the Superior Landlord reasonably considers to be disproportionate and in any event the Landlord and/or the Superior Landlord shall use all reasonable endeavours to minimise such material adverse effect and the Landlord or the Superior Landlord (as the case may be) shall ensure at all times that the Tenant has reasonable access and supply of services to and use of the Premises and that the Tenant's enjoyment of the Premises is not unreasonably adversely affected.

**7.8 Exclusion of liability**

So far as allowed by Law, the Landlord is not responsible to the Tenant for damage to the Premises or persons or property due to any neglect or default of any occupier of, visitor to or person working in the Premises or any statutory authority or the state or condition of the Premises save where due to the Landlord's negligence or breach of the Landlord's obligations in this Lease;

**7.9 Disputes between Occupants**

The Superior Landlord's Surveyor with the agreement of the Tenant may determine any dispute between the Tenant and any owner occupier or tenant of the Superior Landlord's Estate and the determination is conclusive and binding (save in the case of manifest error) on the Tenant.

**7.10 Sale of Goods**

7.10.1 The Tenant irrevocably appoints the Landlord as its agent to store or dispose of any items left by the Tenant or any other person at the Premises which are there more than 10 days after the end of the Term.

7.10.2 The Landlord after that time may store or dispose of those items as it thinks fit without Liability to the Tenant.

**8. NEW TENANCY**

This Lease is a new tenancy as defined in section 1 of the 1995 Act.

**9. EXCLUSION OF CONTRACTS (RIGHTS OF THIRD PARTIES) ACT 1999**

Save for the Superior Landlord, no person shall be entitled to enforce any provisions of this Lease who would not have been so entitled but for the enactment of the Contracts (Rights of Third Parties) Act 1999.

**10. GOVERNING LAW**

This lease and any dispute or claim arising out of or in connection with it or its subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with the law of England and Wales.

**11. JURISDICTION**

Each party irrevocably agrees that the courts of England and Wales shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this lease or its subject matter or formation (including non-contractual disputes or claims).

**12. EXCLUSION OF SECTIONS 24-28 OF THE 1954 ACT**

12.1 The parties confirm that:

12.1.1 the Landlord served a notice on the Tenant, as required by section 38A(3)(a) of the 1954 Act applying to the tenancy created by this Lease, {not less than fourteen days} before this Lease was entered into;

12.1.2 {the Tenant} OR {name of declarant} who was duly authorised by the Tenant to do so} made a {statutory} declaration dated {date} in accordance with the requirements of section 38A(3)(b) of the 1954 Act; and

12.1.3 there is no Agreement for Underlease to which this Lease gives effect.

12.2 The parties agree that the provisions of sections 24 to 28 of the 1954 Act are excluded in relation to the tenancy created by this Lease.

12.2.1 the Landlord served a notice on the Guarantor, as required by section 38A(3)(a) of the 1954 Act applying to the tenancy to be entered into by the Guarantor pursuant to paragraph 4 of Schedule 1, {not less than fourteen days} before this Lease was entered into; and

12.2.2 {the Guarantor} OR {name of declarant} who was duly authorised by the Guarantor to do so} made a {statutory} declaration dated {date} in accordance with the requirements of section 38A(3)(b) of the 1954 Act.

### **13. GUARANTEE AND INDEMNITY**

13.1 The provisions of Schedule 2 apply.

13.2 If an Act of Insolvency occurs in relation to the Guarantor or any guarantor, or if any guarantor (being an individual) dies or becomes incapable of managing his affairs the Tenant shall, if the Landlord requests, procure that a person of standing acceptable to the Landlord, within 10 days of that request, enters into a replacement or additional guarantee and indemnity of the tenant covenants of this lease in the same form as that entered into by the former guarantor.

13.3 Clause 12.2 shall not apply in the case of a person who is guarantor by reason of having entered into an authorised guarantee agreement.

13.4 For so long as the Guarantor or any guarantor remains liable to the Landlord, the Tenant shall, if the Landlord requests, procure that such guarantor joins in any consent or approval required under this Lease and consents to any variation of the Tenant's Covenants of this Lease.

### **14. OPTION TO RENEW**

14.1 The Landlord grants the Tenant, during the Option Period, an option to take the New Lease.

14.2 The Tenant may exercise the Option at any time during the Option Period by serving an Option Notice on the Landlord. The Option Notice must:

- (a) exercise the Option in respect of the whole of the Premises and not in respect of part only; and
- (b) be signed by the Guarantor, confirming its agreement to guarantee the Tenant's obligations under the New Lease.

14.3 The Landlord covenants:

- (a) with the Tenant to use all reasonable endeavours to seek all necessary consents for the grant of the New Lease; and
- (b) to procure that the Landlord's Conveyancer provides to the Tenant and the Guarantor the counterpart engrossment New Lease no less than 30 working days prior to the Completion Date.

- 14.4 The service of the Option Notice by the Tenant shall be of no effect if, at the Completion Date, there is a subsisting material breach of any of the tenant covenants of this Lease.
- 14.5 If the Option is exercised in accordance with the terms of this clause, the Landlord will grant to the Tenant and the Tenant will accept from the Landlord the New Lease, provided that:
- (a) the Tenant cannot require the Landlord to grant the New Lease to any person other than the Tenant; and
  - (b) no premium is payable for the grant of the New Lease; and
  - (c) subject to clause 14.3 above, the Tenant and Guarantor agree to execute and deliver the counterpart New Lease to the Landlord's Conveyancer at least 10 working days prior to the Completion Date.
- 14.6 The New Lease shall:
- (a) include all of the terms, requirements, covenants and conditions contained in this lease except to the extent that they are inconsistent with the terms of this clause;
  - (b) be for a term of years beginning on and including [DATE] and ending on and including [DATE];
  - (c) be at an annual rent per annum determined pursuant to clause 14 of this Lease and then as revised pursuant to the provisions for rent review in the New Lease;
  - (d) not include an option to renew the New Lease; and
  - (e) include clause 15 of this Lease.
- 14.7 The Landlord will grant the New Lease with full title guarantee.
- 14.8 The parties confirm that:
- (a) the Landlord served a notice on the Tenant, as required by section 38A(3)(a) of the LTA 1954 and which applies to the tenancy to be created by the New Lease, before this lease was entered into; and
  - (b) [the Tenant] **OR** [NAME OF DECLARANT], who was duly authorised by the Tenant to do so, made a statutory declaration dated [ ] in accordance with the requirements of section 38A(3)(b) of the LTA 1954; and
  - (c) the Landlord served a notice on the Guarantor, as required by section 38A(3)(a) of the LTA 1954 and which applies to the tenancy to be entered into by the Guarantor pursuant to the New Lease, [not less than 14 days] before this lease was entered into; and
  - (d) [the Guarantor] **OR** [NAME OF DECLARANT], who was duly authorised by the Guarantor to do so, made a [statutory] declaration dated [ ] in accordance with the requirements of section 38A(3)(b) of the LTA 1954.

- 14.9 If the Option is exercised, the Tenant will pay the Landlord's reasonable legal costs and disbursements on a full indemnity basis incurred in connection with the grant of the New Lease on the Completion Date by direct credit.
- 14.10 Completion of the New Lease will take place on or before
- 14.11 If the Option is not exercised in accordance with the terms of this clause then, immediately after the expiry of the Option Period, the Tenant will remove all entries relating to the Option registered against the Landlord's title to the Property.

**15. REVIEW OF THE RENT FOR THE NEW LEASE**

- 15.1 In this clause, the President is the President for the time being of the Royal Institution of Chartered Surveyors or a person acting on his behalf (**President**), and the Surveyor is the independent valuer appointed pursuant to clause 15.7 (**Surveyor**).
- 15.2 The Rent shall be reviewed on the Review Date to equal:
- (a) the Rent payable on the last day of the Contractual Term of the Previous Lease (being the lease dated [ ] made between Moorfields Eye Hospital NHS Foundation Trust (1) and Meiragtx Limited (2) and Kadmon Corporation LLC (3)) (or which would then be payable but for any abatement or suspension of the Rent or restriction on the right to collect it) or, if greater;
  - (b) the open market rent agreed or determined pursuant to this clause.
- 15.3 The open market rent may be agreed between the Landlord and the Tenant at any time before it is determined by the Surveyor.
- 15.4 If the open market rent is determined by the Surveyor, it shall be the amount that the Surveyor determines is the annual rent (exclusive of any VAT) at which the Property could reasonably be expected to be let:
- (a) in the open market;
  - (b) at the Review Date;
  - (c) on the assumptions listed in clause 15.5; and
  - (d) disregarding the matters listed in clause 15.6.
- 15.5 The assumptions are:
- (a) the Property is available to let in the open market:
    - (i) by a willing lessor to a willing lessee;
    - (ii) as a whole;
    - (iii) with vacant possession;
    - (iv) without a fine or a premium;
    - (v) for a term of 5 years commencing on [ ]; and
    - (vi) otherwise on the terms of this lease other than as to the amount of the Rent but including the provisions for review of the Rent;

- (b) the willing lessee has had the benefit of any rent-free or other concession or contribution which would be offered in the open market at the relevant Review Date in relation to fitting out works at the Property;
- (c) the Property may lawfully be used, and is in a physical state to enable it to be lawfully used, by the willing lessee (or any potential undertenant or assignee of the willing lessee) for any purpose permitted by this lease;
- (d) the Landlord and the Tenant have fully complied with their obligations in this lease;
- (e) if the Property, or any means of access to it or any Service Media serving the Property, has been destroyed or damaged, it has been fully restored;
- (f) no work has been carried out on the Property that has diminished its rental value;
- (g) any fixtures, fittings, machinery or equipment supplied to the Property by the Landlord that have been removed by or at the request of the Tenant, or any undertenant or their respective predecessors in title (otherwise than to comply with any law) remain at the Property; and
- (h) the willing lessee and its potential assignees and undertenants shall not be disadvantaged by any actual or potential exercise of an option to tax under Part 1 of Schedule 10 to the VATA 1994 in relation to the Property.

15.6 The matters to be disregarded are:

- (a) any effect on rent of the fact that the Tenant or any authorised undertenant has been in occupation of the Property;
- (b) any goodwill attached to the Property by reason of any business carried out there by the Tenant or by any authorised undertenant or by any of their predecessors in business;
- (c) any effect on rent attributable to any physical improvement to the Property carried out after the date of this lease, by or at the expense of the Tenant or any authorised undertenant with all necessary consents, approvals and authorisations and not pursuant to an obligation to the Landlord (other than an obligation to comply with any law);
- (d) any effect on rent of any obligation on the Tenant to reinstate the Property to the condition or design it was in before any alterations or improvements were carried out; and
- (e) any statutory restriction on rents or the right to recover them.

15.7 The Surveyor shall be an independent valuer who is a Member or Fellow of the Royal Institution of Chartered Surveyors. The Landlord and the Tenant may, by agreement, appoint the Surveyor at any time before either of them applies to the President for the Surveyor to be appointed. Any application to the President may not be made earlier than three months before the relevant Review Date.

15.8 The Surveyor shall act as an expert and not as an arbitrator. The Surveyor shall determine the open market rent and shall have power to determine any issue involving the interpretation of any provision of this lease, his jurisdiction to determine the matters and issues referred to him

or his terms of reference. The Surveyor's decision shall be given in writing, and the Surveyor shall provide reasons for any determination. The Surveyor's written decision on the matters referred to him shall be final and binding in the absence of manifest error or fraud.

15.9 The Surveyor shall give the Landlord and the Tenant an opportunity to make written representations to the Surveyor and to make written counter-representations commenting on the representations of the other party to the Surveyor. The parties will provide (or procure that others provide) the Surveyor with such assistance and documents as the Surveyor reasonably requires for the purpose of reaching a decision.

15.10 Either the Landlord or the Tenant may apply to the President to discharge the Surveyor if the Surveyor:

- (a) dies;
- (b) becomes unwilling or incapable of acting; or
- (c) unreasonably delays in making any determination.

Clause 15.7 shall then apply in relation to the appointment of a replacement.

15.11 The fees and expenses of the Surveyor and the cost of the Surveyor's appointment and any counsel's fees, or other fees, reasonably incurred by the Surveyor shall be payable by the Landlord and the Tenant in the proportions that the Surveyor directs (or if the Surveyor makes no direction, then equally). If either the Landlord or the Tenant does not pay its part of the Surveyor's fees and expenses within ten working days after demand by the Surveyor then:

- (a) the other party may pay instead; and
- (b) the amount so paid shall be a debt of the party that should have paid due and payable on demand to the party that actually made the payment.

The Landlord and the Tenant shall otherwise each bear their own costs in connection with the rent review.

15.12 If the revised Rent has not been agreed by the Landlord and the Tenant or determined by the Surveyor on or before the relevant Review Date, the Rent payable from that Review Date shall continue at the rate payable at the last day of the Contractual Term of the Previous Lease. No later than five working days after the revised Rent is agreed or the Surveyor's determination is notified to the Landlord and the Tenant, the Tenant shall pay:

- (a) the shortfall (if any) between the amount that it has paid for the period from the Review Date of the New Lease until the Rent Payment Date following the date of agreement or notification of the revised Rent and the amount that would have been payable had the revised Rent been agreed or determined on or before that Review Date; and
- (b) interest at the Interest Rate on that shortfall calculated on a daily basis by reference to the Rent Payment Dates on which parts of the shortfall would have been payable if the revised Rent had been agreed or determined on or before that Review Date and the date payment is received by the Landlord.

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15.13 Time shall not be of the essence for the purposes of this clause.

15.14 If at any time there is a guarantor, the guarantor shall not have any right to participate in the review of the Rent.

15.15 As soon as practicable after the amount of the revised Rent has been agreed or determined, a memorandum recording the amount shall be signed by or on behalf of the Landlord and the Tenant and endorsed on or attached to this lease and its counterpart. The Landlord and the Tenant shall each bear their own costs in connection with the memorandum.

This Lease is executed as a deed and delivered on the date set out at the beginning of this deed



## SCHEDULE 1 – ENCUMBRANCES

1. The matters referred to in the property register and charges register of title number EGL434767
2. The matters referred to in the property register and charges register of title number EGL249920
3. The deed of covenant made between National Car Parks Limited (1) the Landlord (2)
4. An agreement dated 4 July 2000 made between London Borough of Hackney (1) and the Landlord (2) pursuant to S106 of the Town and Country Planning Act 1990
5. A lease made between the Superior Landlord (1) and Propylion Limited of part of the Superior Landlord's Estate comprising Block A
6. A lease made between the Superior Landlord (1) and JF Miller Properties Limited of part of the Superior Landlord's Estate comprising Block H

## SCHEDULE 2 – GUARANTEE AND INDEMNITY

### 1. Guarantee and indemnity

- 1.1 The Guarantor guarantees to the Landlord that the Tenant shall:
- 1.1.1 pay the rents reserved by this Lease and observe and perform the tenant covenants of this Lease and that if the Tenant fails to pay any of those rents or to observe or perform any of those tenant covenants, the Guarantor shall pay or observe and perform them; and
  - 1.1.2 observe and perform any obligations the Tenant enters into in an authorised guarantee agreement made in respect of this Lease (the “Authorised Guarantee Agreement”) and that if the Tenant fails to do so, the Guarantor shall observe and perform those obligations.
- 1.2 The Guarantor covenants with the Landlord as a separate and independent primary obligation to indemnify the Landlord against any failure by the Tenant:
- 1.2.1 to pay any of the rents reserved by this Lease or any failure to observe or perform any of the tenant covenants of this Lease; and
  - 1.2.2 to observe or perform any of the obligations the Tenant enters into in the Authorised Guarantee Agreement.

### 2. Guarantor’s liability

- 2.1 The liability of the Guarantor under paragraphs 1.1.1 and 1.2.1 shall continue until the end of the term, or until the Tenant is released from the tenant covenants of this Lease by virtue of the Landlord and Tenant (Covenants) Act 1995, if earlier.
- 2.2 The liability of the Guarantor shall not be affected by:
- 2.2.1 any time or indulgence granted by the Landlord to the Tenant; or
  - 2.2.2 any delay or forbearance by the Landlord in enforcing the payment of any of the rents or the observance or performance of any of the tenant covenants of this Lease (or the Tenant’s obligations under the Authorised Guarantee Agreement) or in making any demand in respect of any of them; or
  - 2.2.3 any refusal by the Landlord to accept any rent or other payment due under this Lease where the Landlord believes that the acceptance of such rent or payment may prejudice its ability to re-enter the Property; or
  - 2.2.4 the Landlord exercising any right or remedy against the Tenant for any failure to pay the rents reserved by this Lease or to observe or perform the tenant covenants of this Lease (or the Tenant’s obligations under the Authorised Guarantee Agreement); or
  - 2.2.5 the Landlord taking any action or refraining from taking any action in connection with any other security held by the Landlord in respect of the Tenant’s liability to pay the rents reserved by this Lease or observe and perform the tenant covenants of the Lease (or the Tenant’s obligations under the Authorised Guarantee Agreement) including the release of any such security; or

- 2.2.6 a release or compromise of the liability of any one of the persons who is the Guarantor, or the grant of any time or concession to any one of them; or
- 2.2.7 any legal limitation or disability on the Tenant or any invalidity or irregularity of any of the tenant covenants of the Lease (or the Tenant's obligations under the Authorised Guarantee Agreement) or any unenforceability of any of them against the Tenant; or
- 2.2.8 the Tenant being dissolved, or being struck off the register of companies or otherwise ceasing to exist, or, if the Tenant is an individual, by the Tenant dying or becoming incapable of managing its affairs; or
- 2.2.9 without prejudice to paragraph 4, the disclaimer of the Tenant's liability under this lease or the forfeiture of this Lease; or
- 2.2.10 the surrender of part of the Property, except that the Guarantor shall not be under any liability in relation to the surrendered part in respect of any period after the surrender; or

by any other act or omission except an express written release of the Guarantor by the Landlord.

2.3 The liability of each of the persons making up the Guarantor is joint and several.

2.4 Any sum payable by the Guarantor shall be paid without any deduction, set-off or counterclaim against the Landlord or the Tenant.

### **3. Variations and supplemental documents**

3.1 The Guarantor shall, at the request of the Landlord, join in and give its consent to the terms of any consent, approval, variation or other document that may be entered into by the Tenant in connection with this Lease (or the Authorised Guarantee Agreement).

3.2 The Guarantor shall not be released by any variation of the rents reserved by, or the tenant covenants in, this Lease (or the Tenant's obligations under the Authorised Guarantee Agreement) whether or not:

3.2.1 the variation is material or prejudicial to the Guarantor; or

3.2.2 the variation is made in any document; or

3.2.3 the Guarantor has consented, in writing or otherwise, to the variation.

3.3 The liability of the Guarantor shall apply to the rents reserved by and the tenant covenants in this Lease (and the Tenant's obligations under the Authorised Guarantee Agreement) as varied except to the extent that the liability of the Guarantor is affected by section 18 of the Landlord and Tenant (Covenants) Act 1995.

### **4. Guarantor to take a new underlease or make payment**

4.1 If this Lease is forfeited or the liability of the Tenant under this Lease is disclaimed and the Landlord gives the Guarantor notice not later than three months after the forfeiture or the Landlord having received notice of the disclaimer, the Guarantor shall enter into a new underlease of the Property on the terms set out in paragraph 4.2.

- 4.2 The rights and obligations under the new underlease shall take effect from the date of the forfeiture or disclaimer and the new underlease shall:
- 4.2.1 be granted subject to the right of any person to have this Lease vested in them by the court and to the terms on which any such order may be made and subject to the rights of any third party existing at the date of the grant;
  - 4.2.2 be for a term that expires at the same date as the end of the Contractual Term of this Lease had there been no forfeiture or disclaimer;
  - 4.2.3 reserve as an initial annual rent an amount equal to the Rent payable under this Lease at the date of the forfeiture or disclaimer or which would be payable but for any abatement or suspension of the Rent or restriction on the right to collect it (subject to paragraph 5) and which is subject to review on the same terms and date provided this Lease;
  - 4.2.4 be excluded from sections 24 to 28 of the 1954 Act; and
  - 4.2.5 otherwise be on the same terms as this Lease (as varied if there has been any variation).
- 4.3 The Guarantor shall pay the Landlord's reasonable solicitor's costs and disbursements (on a full indemnity basis) and any VAT in respect of them in relation to the new underlease and shall execute and deliver to the Landlord a counterpart of the new underlease within one month after service of the Landlord's notice.
- 4.4 The grant of a new underlease and its acceptance by the Guarantor shall be without prejudice to any other rights which the Landlord may have against the Guarantor or against any other person or in respect of any other security that the Landlord may have in connection with this Lease.
- 4.5 The Landlord may, instead of giving the Guarantor notice pursuant to paragraph 4.1 but in the same circumstances and within the same time limit, require the Guarantor to pay an amount equal to the lower of six months' Rent and the time remaining of the Contractual Term of this lease and the Guarantor shall pay that amount on demand.

## **5. Rent at the date of forfeiture or disclaimer**

If at the date of the forfeiture or disclaimer there is a rent review pending under this Lease, then the initial annual rent to be reserved by the new underlease shall be the greater of:

- 5.1 the Rent previously payable (or which would have been payable but for any abatement or suspension of the Rent or restriction on the right to collect it) under the Lease prior to forfeiture or disclaimer; and
- 5.2 the open market rent of the Property at the relevant Review Date, as determined by the Landlord before the grant of the new underlease.

## **6. Payments in gross and restrictions on the Guarantor**

- 6.1 Any payment or dividend that the Landlord receives from the Tenant (or its estate) or any other person in connection with any insolvency proceedings or arrangement involving the Tenant shall be taken and applied as a payment in gross and shall not prejudice the right of the Landlord to recover from the Guarantor to the full extent of the obligations that are the subject of this guarantee and indemnity.
- 6.2 The Guarantor shall not claim in competition with the Landlord in any insolvency proceedings or arrangement of the Tenant in respect of any payment made by the Guarantor pursuant to this guarantee and indemnity. If it otherwise receives any money in such proceedings or arrangement, it shall hold that money on trust for the Landlord to the extent of its liability to the Landlord.

6.3 The Guarantor shall not, without the consent of the Landlord, exercise any right or remedy that it may have (whether against the Tenant or any other person) in respect of any amount paid or other obligation performed by the Guarantor under this guarantee and indemnity unless and until all the obligations of the Guarantor under this guarantee and indemnity have been fully performed.

**7. Other securities**

7.1 This guarantee and indemnity is in addition to any other security that the Landlord may at any time hold from the Guarantor or the Tenant or any other person in respect of the liability of the Tenant to pay the rents reserved by this Lease and to observe and perform the tenant covenants of this Lease. It shall not merge in or be affected by any other security.

7.2 The Guarantor shall not be entitled to claim or participate in any other security held by the Landlord in respect of the liability of the Tenant to pay the rents reserved by this Lease or to observe and perform the tenant covenants of this Lease.

SIGNATURE PAGE

Executed as a Deed by **Moorfields Eye Hospital National Health Service Foundation Trust** whose Corporate common seal was hereunto affixed in the presence of:

Authorised Signatory:

Authorised Signatory:

Executed as a Deed by **Meiragtx Limited** acting by [Zandy Forbes], a director and [Stuart Naylor], a director:

Director: /s/ Zandy Forbes

Director: /s/ Stuart Naylor

Signed as a Deed on behalf of ) *Signatures*

**Kadmon Corporation LLC** )

a limited liability company )  
formed under the laws of the )  
State of Delaware, USA )

by Steve Gordon ) /s/ Steve Gordon

and Konstantin Poukalov ) /s/ Konstantin Poukalov  
Authorised signatories )

being persons who in )  
accordance with the laws of )  
that territory are acting under )  
the authority of the Company. )

**Consent of Independent Registered Public Accounting Firm**

We consent to the reference to our firm under the caption “Experts” and to the use of our report dated March 29, 2018 (except for Note 6, as to which the date is May 11, 2018) in the Registration Statement (Form S-1 No. 333-000000) and related Prospectus of MeiraGTx Holdings plc for the registration of its ordinary shares.

/s/ Ernst & Young LLP

Stamford, Connecticut

May 14, 2018