Registration No. 333-

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

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

MeiraGTx Holdings plc[1]

(Exact name of registrant as specified in its charter)

England and Wales	**2836**	**Not applicable**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(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)

Alexandria Forbes, Ph.D.
President and Chief Executive Officer
MeiraGTx Holdings plc
430 East 29th Street, 10th Floor
New York, NY 10016
(646) 490-2965

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

Copies to:

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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.

Large accelerated filer	☐	**Accelerated filer**	☐
Non-accelerated filer	☒	**Smaller reporting company**	☐
(Do not check if a smaller reporting company)		**Emerging growth company**	☒

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. ☐

1 Prior to the completion of this offering, we intend to incorporate MeiraGTx Holdings plc, a public limited company under the laws of England and Wales, which will be the direct parent of MeiraGTx Limited and the holding company of the business and will be the issuer of ordinary shares in this offering.

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, nominal value per share	$	$

(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 , 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.

	Per Share	Total
Public offering price	$	$
Underwriting discount(1)	$	$
Proceeds, before expenses, to us	$	$

(1) We refer you to "Underwriting" beginning on page 189 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.

Through and including , 2018 (25 days after the commencement of this offering), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

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, a holding company that will be incorporated 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 will be issuer of ordinary shares in this offering.

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 five 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 most advanced product candidates is below. We retain worldwide development and commercialization rights to all of our product candidates.

Product Candidate	Indication	Development Stage			Upcoming Milestone
		Preclinical	Phase 1/2	Phase 3	
Ophthalmology Programs					
AAV-CNGB3	**Achromatopsia** (*CNGB3*)	Orphan U.S. & EU; RPDD; PRIME[1,2,3,4]			• Phase 1/2 Dosing – Expected Completion:
AAV-CNGA3	**Achromatopsia** (*CNGA3*)				• Phase 1/2 Trial – Expected Inititation:
AAV-RPE65	***RPE65*-Deficiency** (*RPE65*)	Orphan U.S. & EU; RPDD[1,2,3]			• Phase 1/2 Dosing – Expected Completion:
AAV-RPGR	**X-linked RP** (*RPGR*)	Orphan U.S. & EU[1,2]			• Phase 1/2 Dosing – Expected Completion:
AAV-AIPL1	**LCA4** (*AIPL1*)	**Compassionate Use** (Specials License U.K.[5]) Orphan U.S. & EU[1,2]			
Salivary Gland Programs					
AAV-AQP1	**Xerostomia** (*hAQP1*)	Orphan U.S.[1]			• Second Phase 1/2 – Expected Initiation:
AAV-AQP1	**Sjogren's** (*hAQP1*)				• Phase 1/2 Trial – Expected Initiation:
Neurodegenerative Diseases Program					
AAV-UPF1	**ALS** (*UPF1*)				• Phase 1/2 – Expected Initiation:

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. Specials license for compassionate use in the United Kingdom.

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;
- 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 four ongoing clinical programs in IRDs with a fifth program expected to enter clinical development in . We have three Phase 1/2 clinical stage programs, targeting each of achromatopsia, inherited retinal dystrophy caused by mutations in *RPE65*, and X-linked retinitis pigmentosa, with dosing in each of these dose escalation studies expected to be completed in . We also have a compassionate use study ongoing to treat patients with Leber congenital amaurosis 4, or LCA4. 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 clinical trial. We believe use of these natural history studies differentiates our programs by providing well characterized 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*, *RPE65*, *RPGR* and *AIPL1*. The FDA also granted rare pediatric disease designation for our clinical programs treating mutations in *RPE65* and *CNGB3* and we have received PRIME designation for our clinical program treating mutations in *CNGB3* from the EMA.

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 multiple inherited eye conditions, we also believe it has potential to be applied to the development of gene-based therapies for other ocular 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 1/2 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 of these patients 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 amyotrophic lateral sclerosis, or 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 . 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 five 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 five clinical 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-RPE65, AAV-RPGR 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 we expect 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 29th Street, 10th Floor, New York, New York 10016 and our telephone number is (646) 490-2965. Our website address is *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 intend to incorporate MeiraGTx Holdings plc, a public limited company under the laws of England and Wales, which will be 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, the historical consolidated financial statements of MeiraGTx Holdings will be retrospectively adjusted to include the historical financial results of MeiraGTx Limited for all periods presented.

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-RPE65, AAV-RPGR 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 ordinary shares outstanding as of , including unvested restricted shares subject to repurchase, and excluding:

- ordinary shares issuable upon exercise of share options outstanding under our 2016 Equity Incentive Plan, referred to as our 2016 Plan, as of , at a weighted-average exercise price of per ordinary share; and
- 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.

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

- the consummation of our corporation reorganization prior to the closing of this offering;
- no exercise of outstanding options after ; 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 and the consolidated balance sheet data as of December 31, 2017 from our audited consolidated financial statements included elsewhere in this prospectus. 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.

	Year Ended December 31,	
	2016	2017
Consolidated Statement of Operations and Comprehensive Loss Data:		
Operating expenses:		
General and administrative	$ 6,026,529	$ 9,325,017
Research and development	14,037,918	22,359,712
Total operating expenses	20,064,447	31,684,729
Loss from operations	(20,064,447)	(31,684,729)
Other non-operating income (expense):		
Foreign currency gain	265,543	1,676,117
Convertible note inducement expense	—	(553,500)
Change in fair value of warrant liability	—	(465,633)
Interest income	32,068	26,073
Interest expense	(25,440)	(42,863)
Net loss	(19,792,276)	(31,044,535)
Net loss attributable to non-controlling interest in subsidiary	305,883	—
Net loss attributable to MeiraGTx shareholders	(19,486,393)	(31,044,535)
Other comprehensive loss	(671,391)	(1,361,365)
Comprehensive loss	(20,157,784)	(32,405,900)
Less: comprehensive loss (income) attributable to non-controlling interest	8,520	—
Comprehensive loss attributable to MeiraGTx shareholders	$(20,149,264)	$(32,405,900)
Net loss attributable to MeiraGTx shareholders	$(19,486,393)	$(31,044,535)
Accretion on Series C preferred shares	(85,425)	(806,963)
Adjusted net loss attributable to MeiraGTx ordinary shareholders	$(19,571,818)	$(31,851,498)
Basic and diluted net loss per ordinary share attributable to ordinary shareholders(1)	$ (0.63)	$ (0.96)
Weighted-average number of ordinary shares outstanding—basic and diluted(1)	31,098,591	33,269,157

(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 December 31, 2017		
	Actual	Pro Forma(1)	Pro Forma As Adjusted(2) (3)
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 8,548,638	$	$
Total assets	25,854,219		
Total liabilities	(21,880,853)		
Total shareholders' (deficit) equity	(47,365,265)		

(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 in each year since inception, including net losses of approximately $31.0 million and $19.8 million for the years ended December 31, 2017 and December 31, 2016, respectively. As of December 31, 2017, we had an accumulated deficit of approximately $65.4 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 December 31, 2017, our cash and cash equivalents were $8.6 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;

- 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.

We are heavily dependent on the success of our most advanced product candidates, AAV-CNGB3, AAV-CNGA3, AAV-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR and AAV-AQP1, which may never occur. We cannot be certain that AAV-CNGB3, AAV-CNGA3, AAV-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR 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;

- 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 the Company's 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 for the years 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

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;

- 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;

- 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. We plan to submit a response to the FDA, and our IND for AAV-CNGB3 will remain on clinical hold until lifted by the FDA. 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-RPE65, AAV-RPGR 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, in the future we may seek and fail to obtain access to the PRIME scheme by the EMA 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 designation 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.

In 2012, the FDA established a breakthrough therapy designation which is intended to expedite the development and review of product candidates that treat serious or life-threatening diseases where 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. The designation of a product candidate as a breakthrough therapy provides potential benefits that include but are not limited to more frequent meetings with the FDA to discuss the development plan for the product candidate and 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. Drugs and biologics designated as breakthrough therapies by the FDA are also eligible for accelerated approval. 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 was admitted to the PRIME scheme of the EMA.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. We cannot be sure that our evaluation of our product candidates as qualifying for breakthrough therapy designation will meet the FDA's expectations. In any event, the receipt of a 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 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.

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-RPE65, AAV-RPGR 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. 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;
- 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, 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 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;
- 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-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR and AAV-AQP1, we may be forced to delay the potential commercialization of AAV-CNGB3, AAV-CNGA3, AAV-RPE65, AAV-RPGR and AAV-AQP1 or reduce the scope of our sales or marketing activities for AAV-CNGB3, AAV-CNGA3, AAV-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR 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.

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-RPE65, AAV-RPGR 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-RPE65, AAV-RPGR 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 manufactures. 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.

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;
- 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;
- 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 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 29, 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 Alexandra 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 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 we 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;
- 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 shares of 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 shares of our ordinary shares in this offering, you 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 shares 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 shares of 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.

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

We are incorporated under English law. The rights of holders of ordinary shares are governed by English law, including the provisions of the U.K. Companies Act 2006, or the Companies Act, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations. See "Description of Share Capital and Articles of Association—Differences in Corporate Law" and "Description of Share Capital and Articles of Association—Articles of Association—Other U.K. Law Considerations—City Code on Takeovers and Mergers." in this prospectus for a description of the principal differences between the provisions of the Companies Act 2006 applicable to us and, for example, the Delaware General Corporation Law relating to shareholders' rights and protections.

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 $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.

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.

Claims of U.S. civil liabilities may not be enforceable against us.

We are incorporated under English law. A substantial portion of our assets are located outside the United States. A part of our senior management and board of directors reside outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon such persons or to enforce judgments obtained in U.S. courts against them or us, including judgments predicated upon the civil liability provisions of the U.S. federal securities laws. The United States and the United Kingdom do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in the United Kingdom. In addition, uncertainty exists as to whether English courts would entertain original actions brought in the United Kingdom against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U.S. courts would be treated by the courts of the United Kingdom as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that certain requirements are met. Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the U.S. securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision. If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement. As a result, U.S. investors may not be able to enforce against us or our senior management, board of directors, or certain experts who are residents of the United Kingdom or countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

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 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.

Transfers of our ordinary shares may be subject to U.K. stamp duty or U.K. stamp duty reserve tax, which we refer to as SDRT, which would increase the cost of dealing in our ordinary shares.

U.K. stamp duty and/or SDRT are imposed in the U.K. on certain transfers of or agreements to transfer chargeable securities (which include shares in companies incorporated in the U.K.) at a rate of 0.5% of the amount or value of the consideration paid for the transfer. Certain issues or transfers of shares to depositaries or into clearance services, as discussed below, are charged at a higher rate of 1.5% unless (in the case of a clearance service) an election has been made under section 97A of the U.K. Finance Act 1986. We understand that the Depository Trust & Clearing Corporation, which we refer to as DTC, has not made such an election. The purchaser or transferee of shares will generally be responsible for paying any stamp duty or SDRT payable.

Transfers of shares, or agreements to transfer shares, held in book entry form through DTC should not be subject to U.K. stamp duty or SDRT in the U.K. A transfer of title in the shares or an agreement to transfer the shares from within the DTC system out of DTC and any subsequent transfers or agreements to transfer that occur entirely outside the DTC system, including repurchase by us, will generally be subject to U.K. stamp duty or SDRT at a rate of 0.5% of any consideration, which is payable by the transferee of the shares. Any such duty must be paid (and the relevant transfer document stamped by Her Majesty's Revenue & Customs, which we refer to as HMRC) before the transfer can be registered in our company books. If such shares are redeposited into the DTC system, the redeposit will attract U.K. stamp duty or SDRT at the higher 1.5% rate.

HMRC has confirmed that it will no longer seek to apply the 1.5% U.K. stamp duty or SDRT charge when new shares of companies incorporated in the U.K. are first issued to a clearance service (or its nominee) or depositary (or its nominee or agent) anywhere in the world. Accordingly, it is not currently expected that U.K.

stamp duty and/or SDRT would be imposed under current U.K. tax law and HMRC published practice on a future issue of our ordinary shares. However, it is possible that the U.K. government may change the relevant law or that DTC may make an election under section 97A of the U.K. Finance Act 1986, and that this may have a material effect on the cost of our share issues and potentially on the cost of dealing in our ordinary shares.

We have significant net operating losses ("NOL") 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, the Company had federal and state NOL carryforwards in the United States of approximately $7,820,000 and $7,779,000, respectively, and cumulative carryforward tax losses in the United Kingdom of approximately $39,971,000, which we expect to be 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. carryforward tax losses will continue indefinitely, subject to relevant restrictions, 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 and U.K. carryforward tax losses are subject to review and possible adjustment by the U.S., U.K. and state tax authorities. NOL carry forwards 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 the Company can utilize annually to offset future taxable income or tax liabilities. 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 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-RPE65, AAV-RPGR 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. Under English law, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated realized profits that have not been previously distributed or capitalized less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2017, 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 December 31, 2017		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
Cash and cash equivalents	$	$	$
Warrant liability	$	$	$
Series C preferred shares, $ nominal value per share; 19,428,037 shares authorized, issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted			
Shareholders' (deficit) equity:			
A Ordinary shares, $ nominal value per share; shares authorized, 34,254,578 shares outstanding, actual; shares authorized, pro forma and pro forma as adjusted; shares outstanding, pro forma; shares outstanding, pro forma as adjusted			
Capital in excess of nominal value			
Accumulated and other comprehensive loss			
Accumulated deficit			
Total shareholders' (deficit) equity			
Total capitalization	$	$	$

(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.

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

- ordinary shares issuable upon exercise of share options outstanding under our 2016 Plan as of December 31, 2017, at a weighted-average exercise price of 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 December 31, 2017, we had a historical net tangible book value of $ million, or $ 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 December 31, 2017.

Our pro forma net tangible book value as of December 31, 2017 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 December 31, 2017, 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 December 31, 2017 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 December 31, 2017	$	
Increase per ordinary share attributable to the conversion of our preferred shares		
Pro forma net tangible book value per ordinary share as of December 31, 2017		
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 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 December 31, 2017, 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 Per Share
	Number	Percent	Number	Percent	
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 December 31, 2017 (which included shares of 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:

- ordinary shares issuable upon exercise of share options outstanding under our 2016 Plan as of December 31, 2017, at a weighted-average exercise price of $ 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 December 31, 2017, 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 and the consolidated balance sheet data as of December 31, 2016 and 2017 from our audited consolidated financial statements appearing at the end of this prospectus.

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

	Year Ended December 31,	
	2016	2017
Consolidated Statement of Operations and Comprehensive Loss Data:		
Operating expenses:		
General and administrative	$ 6,026,529	$ 9,325,017
Research and development	14,037,918	22,359,712
Total operating expenses	20,064,447	31,684,729
Loss from operations	(20,064,447)	(31,684,729)
Other non-operating income (expense):		
Foreign currency gain	265,543	1,676,117
Convertible note inducement	—	(553,500)
Change in fair market value of warrant liability	—	(465,633)
Interest income	32,068	26,073
Interest expense	(25,440)	(42,863)
Net loss	(19,792,276)	(31,044,535)
Net loss attributable to non-controlling interest in subsidiary	305,883	—
Net loss attributable to MeiraGTx shareholders	(19,486,393)	(31,044,535)
Other comprehensive loss	(671,391)	(1,361,365)
Comprehensive loss	(20,157,784)	(32,405,900)
Less: comprehensive loss (income) attributable to non-controlling interest	8,520	—
Comprehensive loss attributable to MeiraGTx shareholders	$ (20,149,264)	$ (32,405,900)
Net loss attributable to MeiraGTx ordinary shareholders	$ (19,486,393)	$ (31,044,535)
Accretion on Series C preferred shares	(85,425)	(806,963)
Adjusted net loss attributable to MeiraGTx ordinary shareholders	$ (19,571,818)	$ (31,851,498)
Basic and diluted net loss per ordinary share attributable to ordinary shareholders(1)	$ (0.63)	$ (0.96)
Weighted-average number of ordinary shares outstanding—basic and diluted(1)	31,098,591	33,269,157

(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 December 31,	
	2016	2017
Consolidated Balance Sheet Data:		
Cash and cash equivalents	$ 17,476,641	$ 8,548,638
Total assets	22,551,149	25,854,219
Total liabilities	6,856,572	21,880,853
Total shareholders' deficit	(17,139,083)	(47,365,265)

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.

We intend to incorporate MeiraGTx Holdings plc under the laws of England and Wales 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, the historical consolidated financial statements of MeiraGTx Holdings will be retrospectively adjusted to include the historical financial results of MeiraGTx Limited for all periods presented.

Overview

We are a vertically integrated, clinical stage gene therapy company with five 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 December 31, 2017, we received gross proceeds of approximately $60.8 million from sales of our Series C preferred shares. In addition, from January 1, 2018 through March 29, 2018, we issued 16,943,396 shares of our Series C preferred shares for gross proceeds of $45.8 million. As of December 31, 2017, we had cash and cash equivalents of $8.5 million.

We are a clinical stage company and have not generated any product revenues to date. We have five clinical programs and a pipeline of preclinical programs. Since inception, we have incurred significant operating losses. Our net losses for the years ended December 31, 2016 and 2017 were $19.5 million and $31.1 million, respectively. As of December 31, 2017, we had an accumulated deficit of $65.5 million. We do not expect to generate revenue from sales of any products for several years, if at all.

Our total operating expenses 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.

- 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,		
	2016	2017	Change
Ophthalmology programs	$ 2,026,592	$ 4,133,015	$ 2,106,423
Salivary gland programs	967,745	913,706	(54,039)
Neurodegenerative diseases programs	922,127	2,220,843	1,298,716
Manufacturing	379,656	3,213,861	2,834,205
Other research and development costs	9,741,798	11,878,287	2,136,489
Total research and development expenses	$ 14,037,918	$ 22,359,712	$ 8,321,794

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 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 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 corporation, 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 $7.7 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.

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.

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 and $1.45 per share as of December 31, 2016, September 15, 2017 and December 31, 2017, 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;
- 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, except in the event of a change of control, which is outside our control and requires shareholder approval. The redemption value of the Series C preferred shares upon a change in control is equal to its liquidation value.

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 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:

	Year Ended December 31,		
	2016	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	$ (19,792,276)	$ (31,044,535)	$ (11,252,259)

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 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.

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 December 31, 2017, we had $8.5 million in cash and cash equivalents.

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

	Year Ended December 31,	
	2016	2017
Net cash used in operating activities	$ (14,809,001)	$ (17,733,918)
Net cash used in investing activities	(2,593,584)	(10,535,717)
Net cash provided by financing activities	20,757,202	19,340,215
Increase (decrease) in cash	$ 3,354,617	$ (8,929,420)

Operating Activities

During the year ended December 31, 2016, our cash used in operating activities of $14.8 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, was partially offset by decreases in current assets, consisting of prepaid expenses, restricted cash 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 $17.7 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 deferred rent and due to affiliate, increased by $11.1 million, was partially offset by decreases in current assets, consisting of prepaid expenses, restricted cash and other current assets, in the amount of $0.8 million.

Investing Activities

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 $20.8 and $19.3 million for the year ended December 31, 2016 and December 31, 2017, respectively, representing proceeds from the issuance of our Series C preferred shares, warrants and notes payable.

Funding Requirements

Our operating expenses have 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.

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.

Contractual Obligations and Commitments

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

		Payments Due by Period			
Contractual Obligation	Total	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	$5,087,813	$2,777,280	$1,712,269	$ 598,264	$ —

(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 five 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.

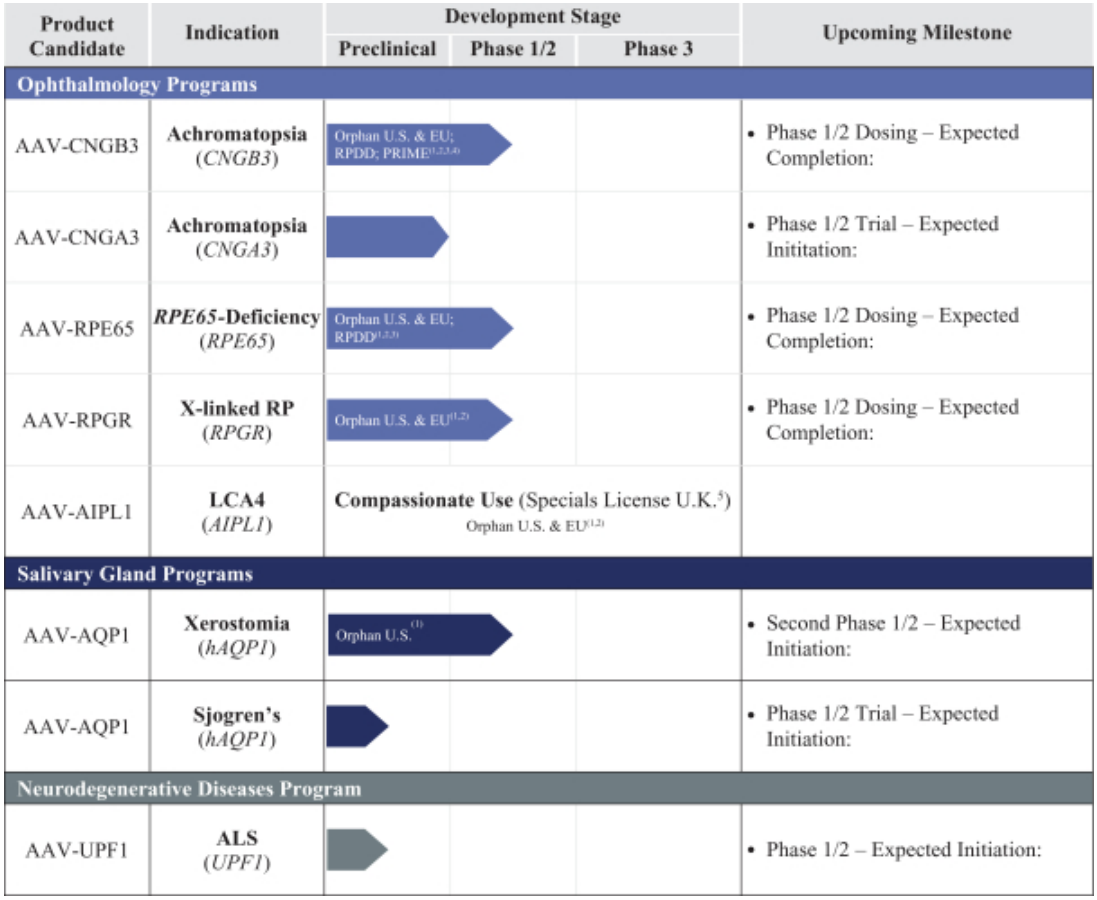
We are also developing a potentially transformative technology to enable the use of small molecules to turn gene therapy product candidates on and off. The aim of this gene regulation platform is to convert gene therapy into a generalizable delivery mechanism for biologic drugs using a small molecule “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.

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



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. Specials license for compassionate use in the United Kingdom.

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;
- 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 four ongoing clinical programs in IRDs, with a fifth program expected to enter clinical development in . We have three Phase 1/2 clinical stage programs, targeting each of achromatopsia, or ACHM, inherited retinal dystrophy caused by mutations in *RPE65*, or *RPE65*-deficiency, and X-linked retinitis pigmentosa, or XLRP, with dosing in each of these dose escalation trials expected to be completed in 2018. We also have a compassionate use study ongoing to treat patients with Leber congenital amaurosis 4, or LCA4. 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 clinical trial. We believe use of these natural history studies differentiates our programs by providing well characterized 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*, *RPE65*, *RPGR* and *AIPL1*. The FDA has also granted rare pediatric disease designation for our clinical programs treating mutations in *RPE65* and *CNGB3*, and we have received PRIME designation for our clinical program treating mutations in *CNGB3* from the EMA.

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 multiple inherited eye conditions, we also believe it has potential to be applied to the development of gene therapies for other ocular 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 1/2 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 of these patients 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 amyotrophic lateral sclerosis, or ALS, and we expect to file an investigational new drug application, or IND, and initiate a clinical trial of our first neurodegenerative disease product candidate in . 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 five 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 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 five clinical 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;

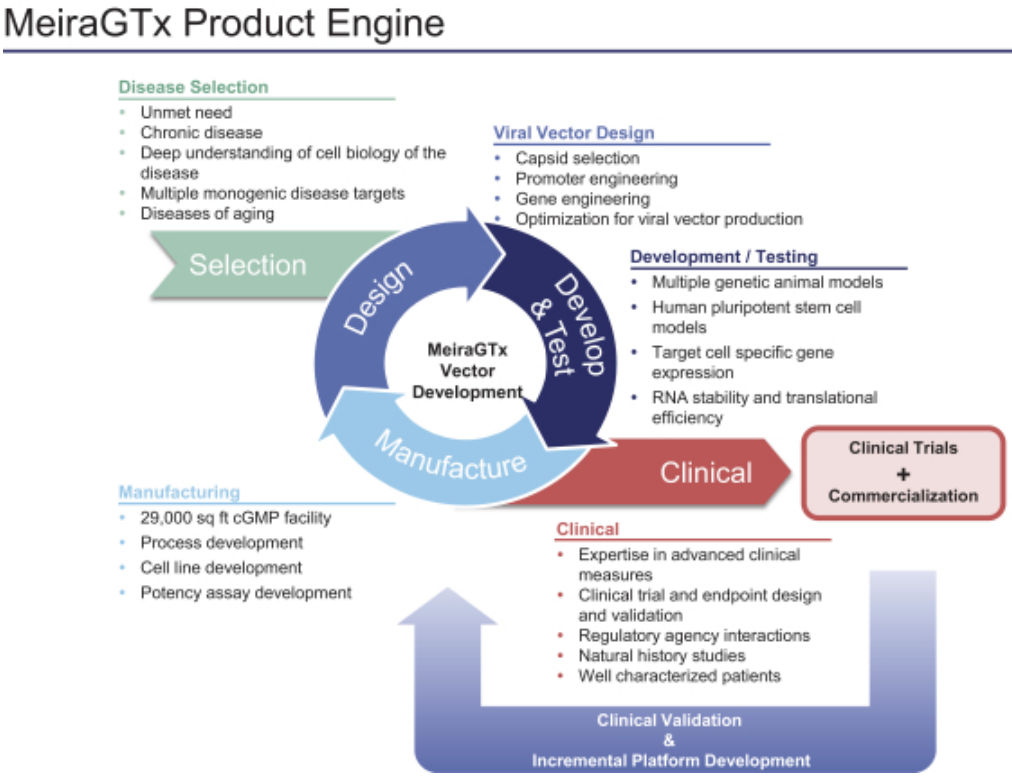
- continue to advance the development of our pipeline of product candidates for the treatment of neurodegenerative disorders;

- 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:



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 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 four clinical programs targeting IRDs, including three ongoing Phase 1/2 clinical trials, in achromatopsia, *RPE65*-deficiency and XLRP, with an additional program expected to enter clinical development in . 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.
- 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.

Our two most advanced product candidates are targeting IRD indications in achromatopsia caused by mutations in the *CNGB3* gene and *RPE65*-deficiency. 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.

Our next IRD indication is XLRP, in which 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 program. The aim of our XLRP 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 . 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 allowed 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. 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 data on each patient for the purpose of post-treatment baseline comparisons. We seek to address this problem by sponsoring prospectively designed natural history studies in each of our Phase 1/2 indications. These studies not only provide a source of potential patients with particular genotypes for our treatment studies, but the patients are well characterized with detailed structural maps of the retina, as well as detailed functional readouts for up to five years in advance of our treatment studies. The natural history studies have also facilitated efficient enrollment of our treatment studies.

In addition to these natural history studies, we have longstanding relationships 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. These institutions are among the premier treatment centers for these indications globally and provide us with access to potential patients for our clinical trials and experts in IRDs who offer guidance and expertise for our development strategy.

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 photophobia, 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.

Our Gene Therapy Program

We have designed specific 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 disabling

symptom of ACHM, which lasts throughout life, is photophobia. We believe it is possible that restoration of cone function in adult patients might have an impact on photophobia 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

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 to respond to light. *CNGB3* is a gene exclusively expressed in cones and our aim is to replace the mutant *CNGB3* gene with a normal copy of the gene in cones of IRD patients' retinas 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 human cone arrestin promoter to drive the expression of a codon optimized *CNGB3* cDNA. Codon optimization improves protein expression by increasing translation efficacy. To transfect cone photoreceptors, we use the AAV8 capsid, which targets these cells and delivers 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.

In our preclinical studies of mice lacking the *Cngb3* gene, we observed that delivering our *CNGB3* product candidate, AAV-CNGB3, via subretinal injection was associated with a restoration of cone function to near normal levels. We also conducted preclinical toxicology and biodistribution studies of AAV-CNGB3 in two animal species and observed no harmful effects on the retina at three and six months after treatment.

In one of our preclinical studies of the effects of subretinal injection of AAV-CNGB3 in mice lacking the *Cngb3* gene, we measured retinal response to light. Figure 1 show the electrical 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 *Cngb3* gene (Figure 1B) and retinas of mutant mice lacking the *Cngb3* gene, but treated with AAV-CNGB3 (Figure 1C). We observed that the response to a bright light pulse was largely absent in the mutant mouse retina, as this response is largely mediated by the cones and is therefore severely impacted by the *Cngb3* mutation (Figure 1B). We also observed that treatment with AAV-CNGB3 was associated with a high-degree of restored function of the cones in these mutant mice 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 electrical signals from rapid flickers. We observed that registering rapid flickers was also impacted by the *Cngb3* mutation (Figure 1B') and this cone flicker response was nearly completely restored in the mutant mouse retina following treatment with AAV-CNGB3 (Figure 1C').

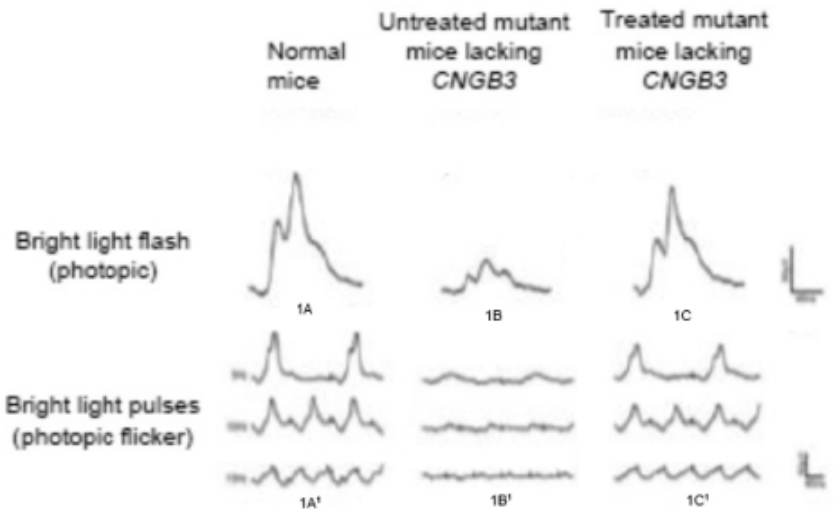


Figure 1. Electrical responses of the retina reacting to two different light stimuli: a single flash of bright light and repeat pulses of bright light at increasing frequency, or flickers.

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-CNGA3 reacting to a flash of bright light and flickers. Treatment with AAV-CNGB3 was associated with a high degree of restoration of function of mutant cones, with the electrical response to a bright flash of light and rapid flickers nearly matching the response of the normal retina.

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

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. We believe access to this large population of well characterized 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 in our meeting following the completion of the Phase 1/2 clinical trial for discussion of our pivotal trial design and path to regulatory approval. In addition to giving us access to well characterized patients and potentially accelerated enrollment in our treatment studies, 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.

This trial is open in the United Kingdom under our CTA. We submitted our IND to the FDA in the fourth quarter of 2017. We received a question from the FDA around our injection device compatibility assay, thus putting our AAV-CNGB3 IND on clinical hold. We plan to submit a response to the FDA, and our IND for AAV-CNGB3 will remain on clinical hold until it is lifted by the FDA. We may not initiate any clinical trials of

AAV-CNGB3 in the United States unless and until the hold is lifted. As of , we had treated patients in this trial at the Moorfields Eye Hospital in London, including patients at the highest proposed dose. We anticipate completing dosing in our *CNGB3* Phase 1/2 clinical trial, including the pediatric dosing, by . We will close out this trial six months after the last patient has been treated. Patients will then move onto a long term follow up study in which patients are followed for safety and indication of benefit for an additional four and a half years. We expect to meet with the regulatory agencies in to discuss the pivotal trial design and path to regulatory approval, with the aim of initiating a pivotal trial in *CNGB3* in .

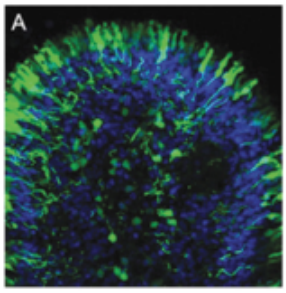
Our *CNGB3* gene therapy product candidate, AAV-CNGB3, was granted orphan drug designation by the FDA and EMA, as well as rare pediatric disease designation by the FDA and PRIME designation by the EMA**,** for the treatment of achromatopsia caused by mutations in the *CNGB3* gene.

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 have designed a synthetic promoter to drive high levels of gene expression. 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 University College of London Hospital, or 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.

We conducted an *in vitro* study to measure the gene expression driven by our cone specific promoter in human cones using HMRs. Figure 2A 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 our promoter drives gene expression in all cone subtypes, we overlaid GFP expression from our promoter with markers specific to each of the cone types. Figure 2B is an image of an S/blue cone and Figure 2C 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 2B’ and 2C’ show the overlay of these cone-specific markers with GFP expression resulting from administration of our promoter, indicating that our promoter drives gene expression in all cone subtypes in this HMR.



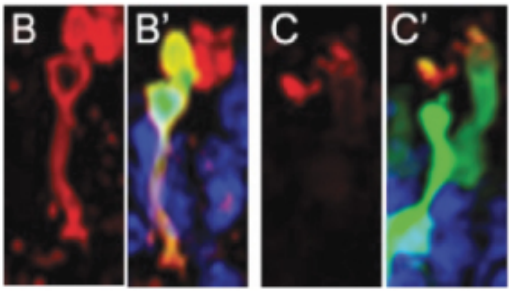


Figure 2A. An hPSC derived HMR showing GFP expression driven by our promoter in human cones.

Figure 2B. The red marker identifies this cone as an S/blue cone.

Figure 2B'. An overlay of GFP expression from our promotor 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 2C. The red marker identifies M/red and L/green cones.

Figure 2C'. An overlay of GFP expression from our promotor 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 mice lacking the *Cnga3* gene, AAV-CNGA3 was associated with a high-degree of restoration of the cone electrical response following subretinal delivery. This rescue of cone function was observed with doses spanning those proposed in the clinical trial and in a dose dependent manner. This supports the evaluation of AAV-CNGA3 to treat patients with ACHM caused by mutations in *CNGA3* in a Phase 1/2 clinical trial.

We aim to initiate a Phase 1/2 dose escalating trial of AAV-CNGA3 in . We expect this clinical trial will have the same design as our *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.

As with our *CNGB3* program, we have a well characterized population of *CNGA3* patients in an ongoing natural history study that includes over 90 participants. This study allows us to collect structural and functional data on prospectively defined endpoints. We expect this natural history study will facilitate enrolment of patients in this Phase 1/2 clinical trial and provide prospective baseline data for the trial.

***RPE65*-Deficiency**

Disease Background and Market Opportunity

RPE65-deficiency, causes rod photoreceptor dysfunction and impaired vision from birth. *RPE-65*-deficiency occurs in approximately one in 125,000 people in the United States. 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 which support the 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.

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. Multiple clinical trials, including one conducted by our collaborators at UCL, have shown that replacing the mutant *RPE65* gene with a normal copy of the gene results in improved nighttime vision in affected children and young adults, demonstrating 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 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 Robin Ali, Ph.D., our head of preclinical ophthalmology, and the team at UCL, we 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.

Optimization of AAV2/5 compared to AAV2/2	
Transfection Efficiency	Changing the capsid to from AAV2/2 to AAV2/5 was associated with the transfection efficiency of RPE to improve 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 also conducted preclinical toxicology and biodistribution studies of AAV-RPE65 in two animal species and observed no harmful effects on the retina at three and six months after treatment.

A Phase 1/2 clinical trial of AAV-RPE65 in both adult and pediatric patients is ongoing. 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 and detailed structural analysis of the retina.

We have an ongoing natural history study in *RPE65*-deficiency that allows us to collect structural and functional data on prospectively defined endpoints. 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.

This clinical trial is enrolling patients in the United Kingdom under our CTA, as well as the United States under our IND. As of we have treated patients in this clinical trial. We anticipate

completing dosing in our *RPE65* Phase 1/2 clinical trial, including the pediatric dosing, in 2018. We will close out this trial six months after the last patient has been treated. Patients will then move onto a long term follow up study in which patients are followed for safety and an indication of benefit for an additional four and a half years.

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

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 early onset in childhood and rapid progression to blindness by the time patients reach 20 to 30 years old . The most frequent mutation causing XLRP is in the retinitis pigmentosa GTPase regulator gene, or *RPGR*, accounting for more than 70% of cases of XLRP and up to 20% of all cases of RP.

The RPGR protein has an essential role in the visual cycle and 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. 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 the most common form of XLRP caused by mutations in the eye specific form of the *RPGR* gene 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 AAV2/5 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 our preclinical studies, we observed AAV-RPGR was associated with rescue of the *Rpgr* mutant phenotype in mice that completely lacked the RPGR protein. Subretinal injection of AAV-RPGR was observed to restore the levels, localization and function of RPGR protein in mutant mice lacking the *Rpgr* gene. We observed the restoration and localization of photosensitive proteins in the photoreceptors, and reduction of long-term retinal degeneration in these animals. In addition, 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 *RPGR*-deficient patients, slowing or halting the degeneration that leads to blindness in these patients.

In one of our preclinical studies to determine the effect of subretinal delivery of AAV-RPGR in mice lacking the *Rpgr* gene, we applied different color stains to investigate the restoration of (i) RPGR protein expression, (ii) correct localization of RPGR protein and (iii) RPGR function. Figures 3 and 4 show the retinas from a normal mouse (3A and 4A), retinas from a mutant mouse strain lacking the gene for *Rpgr* (3B and 4B) and retinas from the same mutant mouse strain that lacks the gene for *Rpgr*, but treated with AAV-RPGR (3C and 4C).

The red stain in Figure 3 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 3A shows the localization of RPGR protein within the photoreceptor at the end of the cilium in a normal mouse retina. Figure 3B shows a retina from a mouse lacking the *Rpgr* gene without any green staining, indicating the absence of the RPGR protein. Figure 3C shows a retina from a mouse lacking the *Rpgr* gene that was treated with AAV-RPGR. The green staining at the end of the photoreceptor cilium is similar to the normal mouse retina. Treatment with AAV-RPGR was associated with the restoration of RPGR protein expression and localization within the individual photoreceptor cells consistent with normal RPGR expression.

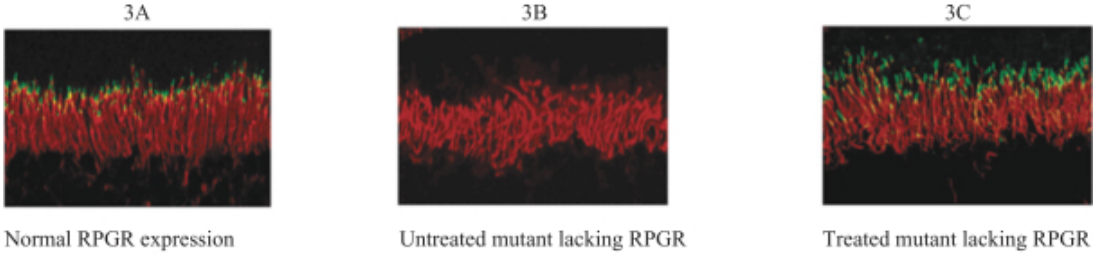


Figure 3. In these preclinical mouse models, the red staining marks a normal protein in the photoreceptor cilia, rootletin, while the green stain reveals localization of RPGR protein within the photoreceptor.

Figure 3A. The retina from a normal mouse

Figure 3B. The retina from a mouse completely lacking the *Rpgr* gene

Figure 3C. The retina from a mouse completely lacking the *Rpgr* gene and treated with AAV-RPGR. The green stain in Figure 3 indicates that RPGR protein expression was restored and was similarly localized within the individual photoreceptor consistent with normal RPGR expression.

Figure 4 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 (4A; 4B; 4C), rhodopsin, and the bottom row shows cone opsin (4A'; 4B'; 4C'). Fully functional RPGR is critical for the correct localization of opsins and Figures 4B and 4B' show that in a *Rpgr* mutant mouse retina the opsins are incorrectly localized. Figures 4C and 4C' show that treatment of these mutant animals with subretinal injection of AAV-RPGR 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.

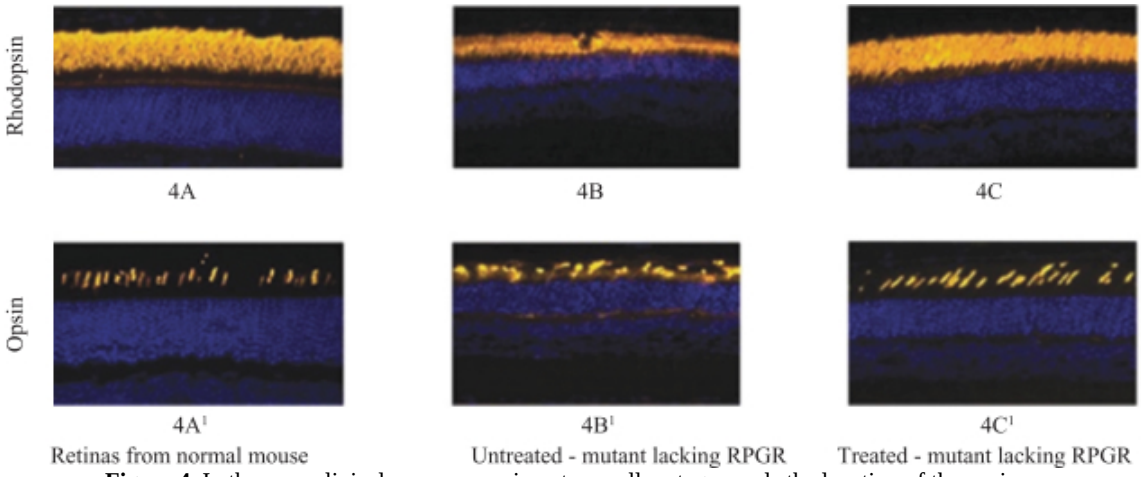


Figure 4. In these preclinical mouse experiments, a yellow tag reveals the location of the opsins.

Figures 4A and 4A'. Normal mouse retina showing the localization of rhodopsin and opsin.

Figures 4B and 4B'. *Rpgr* mutant mouse retina showing the localization of rhodopsin and opsin.

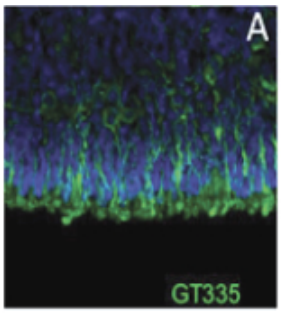
Figures 4C and 4C'. *Rpgr* mutant mouse retina that was treated with AAV-RPGR shows the localization of rhodopsin and opsin. The similar localization between the normal mouse retina and the *Rpgr* mutant mouse retina that was treated with AAV-RPGR indicates that the rhodopsin and opsin are correctly 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 using HMRs derived from patients with the *RPGR* mutation to determine the effect of AAV-RPGR on human photoreceptors. A HMR grown from hPSC from a normal individual is shown in Figure 5A, in which glutamylation of tubulin in normal human photoreceptors is stained in green. Figure 5B shows a HMR derived from a patient lacking *RPGR* and cultured over several months to form many of the anatomic layers of the retina and consisting of all photoreceptor types, while Figure 5C shows the impact of AAV-RPGR treatment on a similarly cultured HMR derived from a patient lacking *RPGR*.

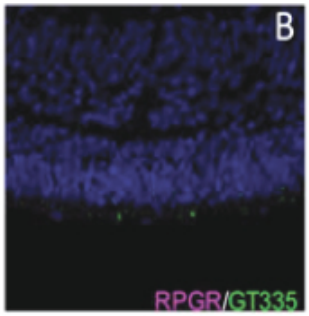
The HMR derived from a *RPGR* patient lacks RPGR protein, making the photoreceptors dysfunctional with no glutamylation of tubulin present. When HMRs from a *RPGR* patient were treated with AAV-RPGR we observed that glutamylation of tubulin returned. We also stained HMRs derived from a *RPGR* patient (Figures 5B and 5C) with a pink marker of RPGR protein. In Figure 5B no pink staining was observed, confirming the lack of RPGR protein. In Figure 5C, when the HMR from a *RPGR* patient was treated with AAV-RPGR, 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 *RPGR* patients, indicates potential clinical utility of AAV-RPGR.



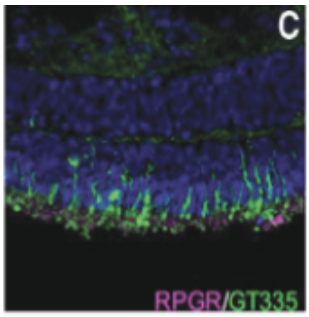
5A

Derived from normal patient



5B

Untreated - Derived from *RPGR* lacking patient



5C

Treated - Derived from RPGR patient

Figure 5. A HMR derived from hPSCs from a normal individual (5A) or a patient lacking *RPGR* (5B and 5C) 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 5A. A HMR derived from normal hPSCs.

Figure 5B. A HMR derived from a patient lacking *RPGR.*

Figure 5C. A HMR derived from a patient lacking *RPGR* that was treated with AAV-RPGR. 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.

We conducted preclinical toxicology and biodistribution studies of AAV-RPGR in two animal species and observed no harmful effects on the retina at three and six months after treatment.

We are conducting a Phase 1/2 clinical trial of AAV-RPGR in both adult and pediatric XLRP patients with mutations in *RPGR-ORF 15*. 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 12 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 and detailed structural analysis of the retina, including structural analysis of individual photoreceptors.

This trial is open in the United Kingdom under our CTA and United States under our IND. We anticipate completing dosing in this Phase 1/2 clinical trial, including the pediatric dosing, in . We will close out this trial 18 months after the last patient has been treated. Patients will then move onto a long term follow up study in which patients are followed for safety and indication of benefit for an additional three and a half years.

We have an ongoing natural history study in XLRP caused by mutations in *RPGR-ORF 15* including approximately 70 patients that allows us to collect structural and functional data for up to five years on prospectively defined endpoints. Access to this population of very well characterized *RPGR* patients has facilitated enrolment of appropriate patients into our Phase 1/2 clinical trial. We will present this natural history data to regulatory agencies in our meeting following the completion of the Phase 1/2 clinical trial for discussion of our pivotal trial design and path to regulatory approval. In addition to giving us access to well characterized patients and potentially accelerated enrollment in our treatment studies, the extensive prospective natural history data on each treated patient may allow us to gather robust data from our Phase 1/2 clinical trial in a condensed timeframe.

The FDA and EMA have granted orphan status to AAV-RPGR for the treatment of retinitis pigmentosa.

LCA4-AIPL1

Disease Background

LCA4-AIPL1 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-AIPL1, 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-AIPL1, 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. Introducing this viral vector in mouse models with the most severe form of the LCA4 showed substantial, long-term improvement in these animals.

We manufactured and released AAV-AIPL1 viral vector for a compassionate use study under a license in the United Kingdom that is now open to treat appropriate LCA4 patients at the Moorfields Eye Hospital in London. We anticipate using the initial data from this trial to inform our discussions with regulatory agencies about subsequent development and potential licensing plans of this product to treat LCA4.

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 angiogeneisis, 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 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 40% of patients who remain cancer free for two or more years after radiation treatment for head and neck cancer suffer from grade 2 or 3 RIX. There are approximately 170,000 of these 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 using adenovirus as the vector to deliver the *hAQP1* to the remaining epithelial cells in the parotid gland of patients suffering from chronic RIX. 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 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.

We are currently conducting a Phase 1/2 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. We are using AAV2 to deliver the *hAQP1* gene, as we believe it efficiently transfects the salivary gland cells and does not spread beyond the target cells. The aim of our trial is to determine the safety of inserting *hAQP1* locally into the salivary glands of RIX patients and to measure changes in salivary flow resulting from the introduction of this channel.

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 fives 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. We have also observed improvements in ALS-like symptoms related to limb strength and mobility in rodent models of ALS 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 with the goal of initiating a clinical trial of AAV-UPF1 in ALS patients in .

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 administrated 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 goal is advance this technology and identify product candidates for preclinical development by .

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, or an exclusive option to license 29 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 in the United States, Europe, Australia, Canada, China, India, Japan and 14 other selected countries and regions. Patents issued from this family are expected to expire Feb. 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. 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, relating to our *RPE65* program, includes 17 pending patent applications in the United States, Europe, Australia, Canada, China, India, Japan and ten other selected countries. 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, relating to our *CNGA3* program, 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, relating to our *RPGR* program, 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, relating to our dry AMD gene therapy program, includes 23 pending applications in the United States, Europe, Australia, Canada, China, India, Japan and 16 other selected countries and regions. 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 relating to our ALS gene therapy program. 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 Oct. 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 for *RPE65*, 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 milestone 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 on a country-by-country basis until the expiration of all of our payment obligations in such country under the First UCLB License Agreement or Athena Addendums, as applicable. 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 UCBL 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.

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 6 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 related to our *RPGR* gene therapy program 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 milestone 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 3 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 supercedes 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 for *CNGA3*, related to our *CNGA3* gene therapy program 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 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 milestone 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 UCL'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 relating to our gene therapy program for the treatment of ALS 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. 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.

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 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 PHSA Act emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA

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 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.

Employees

As of March 29, 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.

Executive Officers and Directors

The following table sets forth the name, age and position of each of our executive officers and non-employee directors as of February 28, 2018.

Name	Age	Position
Executive Officers		
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
Non-employee Directors		
Keith R. Harris, Ph.D.	65	Chairman
Ellen Hukkelhoven, Ph.D.	31	Director
Arnold J. Levine, Ph.D.	78	Director
Joel S. Marcus	70	Director
Neil Mendoza	58	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 Corporation, 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, a healthcare hedge fund from September 2000 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, Mr. Giroux was a founding partner and healthcare portfolio manager of Meadowvale Partners, a multi-strategy hedge fund from January 2010 until June 2012. 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, 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, a gene therapy company. Prior to joining Oxford BioMedica, Dr. Naylor focused on translational cancer research at the Institute of Cancer Research. 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, 2016. Dr. Harris is a London-based investment banker and financier with a 25-year career as a senior corporate finance and takeover advisor. Since 2013, 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 at The Cancer Institute of New Jersey, Robert Wood Johnson School of Medicine, and 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, 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 which is a strategic venture arm of Alexandria Real Estate Equities and the managing member of a holder of more than 5% of our outstanding shares. Prior to founding Alexandria Real Estate Equities, 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 Communications, a subsidiary of WPP. 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.

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 Corporation, 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 eight members. Our board of directors has determined that, of our eight 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. 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. Our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of our outstanding voting shares entitled to vote in the election of directors.

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*. 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;
- 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;
- 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*. 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.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Option Awards ($)(2)	All Other Compensation ($)(3)	Total ($)
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,

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 by or 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.

Named Executive Officer	2017 Options Granted
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.

		Option Awards				Stock Awards	
Name	Grant Date	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

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

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:

Name	Fees Earned or Paid in Cash ($)	Total ($)
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.

Name	Options Outstanding (#)
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 .

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

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 MeiraGTx Limited 2016 Equity Incentive Plan, which we refer to as our Prior 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.

In addition, the maximum aggregate grant date fair value as determined in accordance with FASB ASC Topic 718 (or any successor thereto), of awards granted to any non-employee director for services as a director pursuant to the 2018 Plan during any fiscal year may not exceed $ (or, in the fiscal year of any director's initial service, $). The plan administrator may, however, make exceptions to such limit on director compensation in extraordinary circumstances, subject to the limitations in the 2018 Plan.

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.

Foreign Participants, Claw-Back Provisions, Transferability and Participant Payments

The plan administrator may modify awards granted to participants who are foreign nationals or employed outside the United States or establish subplans or procedures to address differences in laws, rules, regulations or customs of such foreign jurisdictions. 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 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 March 2018, we issued an aggregate 36,423,285 Series C preferred shares at a purchase price of $2.70 per share, for aggregate consideration of approximately $97.9 million, to investors.

In April 2016, we issued 230,000 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 Alexandria Venture Investments, LLC, or AVI, 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 Equities No. 7, LLC, or AE7, an affiliated entity of AVI, 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 AE7 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.

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.

Participants	Series A Ordinary Shares	Series C Preferred Shares	Warrants
Directors and Officers			
Alexandria Forbes†	3,320,871	—	—
Richard Giroux†	2,219,271	—	—
Stuart Naylor	1,982,807	—	—
Joel S. Marcus	125,000	185,180	—

† Indicates a Founder

Participants	Series A Ordinary Shares	Series C Preferred Shares	Warrants
5% or Greater Shareholders(1)	—	—	—
Kadmon Corporation, LLC	13,258,200	460,000	2,777,778
Perceptive Life Sciences Master Fund, Ltd	—	6,481,482	900,000
Adena Estate, Inc.	1,250,000	5,555,556	—
Alexandria Equities No. 7, LLC	374,500	5,126,809	—
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:

Director	Principal Shareholder
Alexandria Forbes	Kadmon Corporation, LLC
Thomas E. Shenk	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 ordinary shares. Under the terms of the agreement, Dr. Ali will receive aggregate compensation of £110,000 per year, or approximately $135,000 using 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, 2016 and 2017, the Company recorded £110,000 and £110,000 or approximately $135,000 and $128,000, respectively, using the average exchange rates during the year ended December 31, 2016 and 2017, respectively, in research and development costs under these agreements. Future obligations to be paid under this agreement equal £110,000, or approximately $149,000, using exchange rates as of December 31, 2017.

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, and we have agreed to pay Dr. Waksal annual compensation of $400,000 for the fiscal year ending December 31, 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. As of March 29, 2018, Dr. Waksal held shares representing approximately 3.1% 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 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 to the fullest extent permitted by the laws of England and Wales, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer. 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. In April 2016, we issued 230,000 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, the amount due to Kadmon was $543,038 and $861,030, 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 AV1, AE7 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 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.

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 $120,000 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 February 28, 2018, after giving effect to our corporate reorganization by:

- 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 ordinary shares outstanding as of , 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 , 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. 29th Street, 10th 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.

	Shares Beneficially Owned Prior to Offering		Shares Beneficially Owned After Offering	
Name of Beneficial Owner	**Number**	**Percentage**	**Number**	**Percentage**
5% or Greater Shareholders				
Kadmon Corporation, LLC(1)		%		%
Perceptive Life Sciences Master Fund, Ltd(2)				
Adena Estate, Inc.				
Alexandria Equities No. 7, LLC(3)				
Robin Ali, Ph.D.				
Named Executive Officers and Directors				
Keith R. Harris, Ph.D.(4)				
Alexandria Forbes, Ph.D.(5)				
Ellen Hukkelhoven, Ph.D.(6)				
Arnold J. Levine, Ph.D.(7)				
Joel S. Marcus(8)				
Neil Mendoza(9)				
Stuart Naylor, Ph.D.(10)				
Thomas E. Shenk, Ph.D.(11)				
Richard Giroux(11)				
All executive officers and directors as a group (9 persons)				

* Less than 1%.

(1) 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. The address of Kadmon Corporation, LLC is 450 E. 29th Street, 16th Floor, New York, New York 10016.

(2) Consists of ordinary shares, a warrant to purchase ordinary shares and options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 28, 2018. 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 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 ordinary shares and a warrant to purchase ordinary shares 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. The address for Alexandria Equities, LLC is 385 E. Colorado Blvd., Suite 299, Pasadena, California 91101.

(4) Consists of ordinary shares and options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 28, 2018.

(5) Consists of ordinary shares and options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 28, 2018.

(6) Consists of ordinary shares held by Perceptive Life Sciences Master Fund, Ltd. Dr. Hukkelhoven is a senior analyst at Perceptive Advisors, LLC, which is the investment manager of Perceptive Life Sciences Master Fund, Ltd. Dr. Hukkelhoven 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.

(7) Consists of ordinary shares and options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 28, 2018.

(8) Consists of ordinary shares held by Alexandria Equities No. 7, LLC, ordinary shares held by Third Amended and Restated Joel and Barbara Marcus Family Trust and ordinary shares and options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 28, 2018. Dr. 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, 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.

(9) Consists of ordinary shares and options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 28, 2018.

(10) Consists of ordinary shares and options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 28, 2018.

(11) Consists of ordinary shares held by Double Epiphany, LLC and options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 28, 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.

(12) Consists of ordinary shares and options to purchase ordinary shares that are or will be immediately exercisable within 60 days of February 28, 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 England and Wales 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 will be incorporated pursuant to the laws of England and Wales 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 U.K. Companies Act 2006, or Companies Act.

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. See "—Post-IPO Articles of Association" below;
- general authorization of our directors for purposes of Section 551 of the Companies Act to issue shares in the company and grant rights to subscribe for or convert any securities into shares in the company up to a maximum aggregate nominal amount of for a period of five years; and
- empowering of our directors pursuant to Section 570 of Companies Act to issue equity securities for cash pursuant to the Section 551 authority referred to above as if the statutory preemption rights under Section 561(1) of the Companies Act did not apply to such allotments.

Share Capital

Upon closing of this offering, there will be ordinary shares in issue.

Ordinary Shares

In accordance with our articles of association to be adopted upon the closing of this offering (the "Articles"), the following summarizes the rights of holders of our ordinary shares:

(a) each holder of our ordinary shares is entitled to one vote per ordinary share on all matters to be voted on by shareholders generally;

(b) the holders of our ordinary shares shall be entitled to receive notice of, attend, speak, and vote at our general meetings; and

(c) the holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders.

Registered Shares

We are required by the Companies Act to keep a register of our shareholders. Under English law, the ordinary shares are deemed to be issued when the name of the shareholder is entered in our share register. The

share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our ordinary shares.

Under the Companies Act, we must enter an allotment of ordinary shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect the ordinary shares being sold in the offering. We also are required by the Companies Act to register a transfer of ordinary shares (or give the transferee notice of and reasons for refusal) as soon as practicable and in any event within two months of receiving notice of the transfer.

We, any of our shareholders or any other affected person may apply to the court for rectification of the share register if:

(a) the name of any person, without sufficient cause, is wrongly entered in or omitted from our register of members; or

(b) there is a default or unnecessary delay in entering on the register the fact of any person having ceased to be a member or on which we have a lien, provided that such refusal does not prevent dealings in the shares taking place on an open and proper basis.

Preemptive Rights

English law generally provides shareholders with preemptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders in a general meeting, to exclude preemptive rights. Such an exclusion of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years).

Transfer Agent and Registrar

The transfer agent and registrar for our ordinary shares will be .

Stock Exchange Listing

We intend to apply to have our ordinary shares listed on the Nasdaq Global Market under the symbol “MGTX.”

Key Provisions of the Articles of Association and English Law Considerations

The following is a summary of certain key provisions of the Articles and English law considerations. Please note that this is only a summary and is not intended to be exhaustive. For further information please refer to the full version of the Articles which are included as an exhibit to the registration statement of which this prospectus is a part.

Key Provisions of the Articles of Association

[Reserved]

English Law Considerations

City Code on Takeovers and Mergers

At this time, we do not expect the City Code on Takeovers and Mergers (the "Takeover Code") to apply to us. The Panel on Takeovers and Mergers (the "Takeover Panel") has confirmed to our representatives that, on the basis of our planned board of directors, it does not consider the Takeover Code to apply to the Issuer, although that position is subject to change if our place of central management and control is subsequently found to move to the United Kingdom. If, at the time of a takeover, after the Takeover Panel determines that we have our place of central management and control in the United Kingdom, we could be subject to the Takeover Code, which is issued and administered by the Takeover Panel. The Takeover Code provides a framework within which takeovers of companies subject to it are conducted. In particular, the Takeover Code contains certain rules in respect of mandatory offers. Under Rule 9 of the Takeover Code, if a person:

(a) acquires an interest in our shares that, when taken together with shares in which he or she or persons acting in concert with him or her are interested, carries 30% or more of the voting rights of our shares; or

(b) who, together with persons acting in concert with him or her, is interested in shares that in the aggregate carry not less than 30% and not more than 50% of the voting rights in the Issuer, and such persons, or person acting in concert with him, acquires additional interests in shares that increase the percentage of shares carrying voting rights in which that person is interested,

the acquirer, and, depending on the circumstances, its concert parties, would be required (except with the consent of the Takeover Panel) to make a cash offer for our outstanding shares at a price not less than the highest price paid for any interests in the shares by the acquirer or its concert parties during the previous 12 months.

As noted above, at this time, we do not expect the Takeover Code to apply on the basis that our management and control is outside the United Kingdom. However, the analysis of whether the Takeover Code applies is fact-specific and therefore subject to change.

Mandatory Purchases and Acquisitions

Pursuant to Sections 979 to 991 of the Companies Act, where a takeover offer has been made for us and the offeror has acquired or unconditionally contracted to acquire not less than 90% in value of the shares to which the offer relates and not less than 90% of the voting rights carried by those shares, the offeror may give notice to the holder of any shares to which the offer relates which the offeror has not acquired or unconditionally contracted to acquire that he wishes to acquire, and is entitled to so acquire, those shares on the same terms as the general offer. The offeror would do so by sending a notice to the outstanding minority shareholders telling them that it will compulsorily acquire their shares. Such notice must be sent within three months of the last day on which the offer can be accepted in the prescribed manner. The squeeze-out of the minority shareholders can be completed at the end of six weeks from the date the notice has been given, subject to the minority shareholders failing to successfully lodge an application to the court to prevent such squeeze-out any time prior to the end of those six weeks following which the offeror can execute a transfer of the outstanding shares in its favor and pay the consideration to us, which would hold the consideration on trust for the outstanding minority shareholders. The

consideration offered to the outstanding minority shareholders whose shares are compulsorily acquired under the Companies Act must, in general, be the same as the consideration that was available under the takeover offer.

Sell Out

The Companies Act also gives our minority shareholders a right to be bought out in certain circumstances by an offeror who has made a takeover offer for all of our shares. The holder of shares to which the offer relates, and who has not otherwise accepted the offer, may require the offeror to acquire his shares if, prior to the expiry of the acceptance period for such offer, (i) the offeror has acquired or unconditionally agreed to acquire not less than 90% in value of the voting shares, and (ii) not less than 90% of the voting rights carried by those shares. The offeror may impose a time limit on the rights of minority shareholders to be bought out that is not less than three months after the end of the acceptance period. If a shareholder exercises his rights to be bought out, the offeror is required to acquire those shares on the terms of this offer or on such other terms as may be agreed.

Disclosure of Shareholder Ownership

Under section 793 of the Companies Act, the Issuer may give notice to any person whom the Issuer knows or has reasonable cause to believe (a) to be interested in the shares of the Issuer or (b) to have been so interested at any time during the three years immediately preceding the date on which the notice is issued. The notice may require the person (a) to state whether or not it is the case and (b) if it holds, or has during that time held, any such interest, to give such further information as may be required by the Issuer in accordance with section 793 of the Companies Act. The notice may require the person to give particulars of its present or past interest in the Issuer's shares and the information required by the notice must be given within such reasonable time as may be specified in the notice. Where a notice is served by the Issuer on a person under section 793 of the Companies Act and that person fails to give the Issuer the information required by the notice within the time specified in it, the Issuer may apply to the court for an order directing that the shares in question be subject to restrictions.

Purchase of Own Shares

Under English law, a limited company may only purchase its own shares out of the distributable profits of the company or the proceeds of a fresh issue of shares made for the purpose of financing the purchase, provided that they are not restricted from doing so by their articles. A limited company may not purchase its own shares if, as a result of the purchase, there would no longer be any issued shares of the company other than redeemable shares or shares held as treasury shares. Shares must be fully paid in order to be repurchased.

Subject to the above, we may purchase our own fully paid shares otherwise than on a recognized investment exchange pursuant to a purchase contract authorized by resolution of shareholders before the purchase takes place. Any authority will not be effective if any shareholder from whom we propose to purchase shares votes on the resolution and the resolution would not have been passed if he had not done so. The resolution authorizing the purchase must specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

Distributions and Dividends

Under the Companies Act, before a company can lawfully make a distribution or dividend, it must ensure that it has sufficient distributable reserves (on a non-consolidated basis). The basic rule is that a company's profits available for the purpose of making a distribution are its accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less its accumulated, realized losses, so far as not previously written off in a reduction or reorganization of capital duly made. The requirement to have sufficient distributable reserves before a distribution or dividend can be paid applies to us and to each of our subsidiaries that has been incorporated under English law.

It is not sufficient that we, as a public company, have made a distributable profit for the purpose of making a distribution. An additional capital maintenance requirement is imposed on us to ensure that the net worth of the company is at least equal to the amount of its capital. A public company can only make a distribution:

(a) if, at the time that the distribution is made, the amount of its net assets (that is, the total excess of assets over liabilities) is not less than the total of its called up share capital and undistributable reserves; and

(b) if, and to the extent that, the distribution itself, at the time that it is made, does not reduce the amount of the net assets to less than that total.

Exchange Controls

There are no governmental laws, decrees, regulations or other legislation in the United Kingdom that may affect the import or export of capital, including the availability of cash and cash equivalents for use by us, or which may affect the remittance of dividends, interest, or other payments by us to non-resident holders of our ordinary shares, other than withholding tax requirements. There is no limitation imposed by English law or the Articles on the right of non-residents to hold or vote shares.

Differences in Corporate Law

The applicable provisions of the Companies Act differ from laws applicable to U.S. corporations organized in Delaware and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act applicable to the Issuer and the Delaware General Corporation Law relating to shareholders' rights and protections. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to English law and Delaware law.

	England and Wales	**Delaware**
Number of Directors	Under the Companies Act, a public limited company must have at least two directors and at least one of the directors must be a natural person. Subject to the Companies Act, the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.

	England and Wales	Delaware
Removal of Directors	Under the Companies Act, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided that 28 clear days' notice of the resolution is given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act must also be followed (such as allowing the director to make representations against his or her removal either at the meeting or in writing).	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (i) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, shareholders may effect such removal only for cause, or (ii) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.
Vacancies on the Board of Directors	Under English law, the procedure by which directors (other than a company's initial directors) are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually unless a resolution that more than one director can be appointed has first been agreed to by the meeting without any vote being given against it.	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of shares is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

	England and Wales	Delaware
Annual General Meeting	Under the Companies Act, a public limited company must hold an annual general meeting in each six-month period beginning the day following its accounting reference date.	Under Delaware law, the annual meeting of shareholders shall be held at such place, on such date and at such time as may be designated by or in the manner provided in the certificate of incorporation or bylaws, or if not so designated, as determined by a majority of the board of directors.
General Meeting	Under the Companies Act, a general meeting of the shareholders of a public limited company may be called by the directors. Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings (excluding any paid-up capital held as treasury shares) can require the directors to call a general meeting and, if the directors fail to do so within a certain period, may themselves convene a general meeting.	Under Delaware law, special meetings of the shareholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.

	England and Wales	Delaware
Notice of General Meetings	Under the Companies Act, 21 clear days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 clear days' notice is required for any other general meeting. In addition, certain matters (such as the removal of directors or auditors) require special notice, which is 28 clear days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the shareholders having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.	Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting to the shareholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour and purpose or purposes of the meeting.
Proxy	Under the Companies Act, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, each shareholder entitled to vote at a meeting of shareholders or to express consent or dissent to corporate action in writing without a meeting may authorize another person or persons to act for such shareholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period.

	England and Wales	Delaware
Pre-emptive Rights	Under the Companies Act, “equity securities” (being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution (“ordinary shares”) or (ii) rights to subscribe for, or to convert securities into, ordinary shares) must not be allotted unless: (i) offered first, on the same or more favorable terms, to the existing ordinary shareholders in the company in proportion as nearly as practicable to the respective nominal value of their holdings of ordinary shares and (ii) the period during which any such offer may be accepted has expired or the company has received notice of the acceptance or refusal of every offer so made. Such pre-emption provisions do not apply if: (i) the allotment is of bonus shares or (ii) the allotment is to be wholly or partly paid up otherwise than in cash or (iii) the allotment is pursuant to an employees’ share scheme. Where the directors of a company are generally authorized to allot or grant equity securities in the company, they may be given power by the articles of association or by a special resolution of the company to allot equity securities as if the shareholders’ rights of pre-emption did not apply to the allotment (or with such modifications as the directors may determine).	Under Delaware law, no shareholder shall have any pre-emptive right to subscribe to an additional issue of shares or to any security convertible into such shares unless, and except to the extent that, such right is expressly granted to such shareholder in the certificate of incorporation,.
Authority to Allot	Under the Companies Act, the directors of a company must not allot shares or grant of rights to subscribe for or to convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.	Under Delaware law, if the corporation’s charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of shares. It may authorize capital shares to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.

	England and Wales	Delaware
Liability of Directors and Officers	Under the Companies Act, any provision (whether contained in a company's articles of association or any contract or otherwise) that purports to exempt a director of a company (to any extent) from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company is void. Any provision by which a company directly or indirectly provides an indemnity (to any extent) for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to (a) purchase and maintain insurance against such liability; (b) provide a "qualifying third party indemnity" (being an indemnity against liability incurred by the director to a person other than the company or an associated company as long as he is successful in defending the claim or criminal proceedings); and (c) provide a "qualifying pension scheme indemnity" (being an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan).	Under Delaware law, the certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation or its shareholders for monetary damages for breach of fiduciary duty as a director, provided that such provision shall not eliminate or limit the liability of a director: (i) For any breach of the director's duty of loyalty to the corporation or its shareholders; (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law; (iii) intentional or negligent payment of unlawful dividends or unlawful share purchases or redemptions; or (iv) for any transaction from which the director derived an improper personal benefit.

	England and Wales	Delaware
Voting Rights	Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (a) not fewer than five shareholders having the right to vote on the resolution; (b) any shareholder(s) representing at least 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attached to treasury shares); or (c) any shareholder(s) holding shares in the company conferring a right to vote on the resolution being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll. Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the shareholders present (in person or by proxy) and entitled to vote and voting at a meeting. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of the shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present (in person or by proxy) and entitled to vote at the meeting. If a poll is demanded, a special resolution is passed if it is approved by holders representing not less than 75% of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution.	Under Delaware law, unless otherwise provided in the certificate of incorporation, each shareholder shall be entitled to one vote for each share of capital stock held by such shareholder.

	England and Wales	Delaware
Shareholder Vote on Certain Transactions	The Companies Act provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. The court may order a meeting of the creditors, or class of creditors, or shareholders, or class of shareholders, on an application by (i) the company, (ii) any creditor or shareholder of the company or (iii) the liquidator or administrator of the company. The court may sanction the compromise or arrangement if 75% in value of the creditors or class of creditors or shareholders or class of shareholders (as the case may be), present and voting either in person or by proxy at the meeting summoned, agree a compromise or arrangement. The court's order has no effect until the delivery of the court order to the registrar.	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: (i) the approval of the board of directors; and (ii) approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter.

	England and Wales	Delaware
Standard of Conduct for Directors	Under English law, a director owes various statutory and fiduciary duties to the company, including: (i) a duty to act in accordance with the company's constitution and only exercise powers for the purposes which they are conferred; (ii) a duty to act in the way he or she considers, in good faith, would be most likely to promote the success of the company for the benefit of its shareholders as a whole; (iii) a duty to exercise independent judgment; (iv) a duty to exercise reasonable care, skill and diligence; (v) a duty to avoid a situation in which he or she has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company; (vi) a duty not to accept benefits from third parties conferred by reason of his being a director or doing (or not doing) anything as a director; and (vii) a duty to declare any interest that he or she has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.	Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the shareholders. Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director acts 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 all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, 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. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.

	England and Wales	Delaware
Shareholder Suits	Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder of a company may apply to the court by petition for an order on the ground (a) that the company's affairs are being or have been conducted in a manner that is unfairly prejudicial to the interests of shareholders generally or of some part of its shareholders (including at least himself or herself), or (b) that an actual or proposed act or omission of the company (including an act or omission on its behalf) is or would be so prejudicial.	Under Delaware law, a shareholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must: • state that the plaintiff was a shareholder at the time of the transaction of which the plaintiff complains or that the plaintiff's shares thereafter devolved on the plaintiff by operation of law; and • allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or • state the reasons for not making the effort. Additionally, the plaintiff must remain a shareholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

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 capital stock 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 "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.

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.

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 branch or agency 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.

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. Holders should note that at the Spring Budget on 8 March 2017, the UK Government announced that the annual dividend allowance would be reduced from £5,000 to £2,000 from 6 April 2018.

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 who 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.

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.

Transfers of our ordinary shares within a clearance service or depositary receipt system should not give rise to a liability to stamp duty or SDRT, provided that no instrument of transfer is entered into and that no election that applies to the ordinary shares is, or has been, made by the clearance service under Section 97A of the UK Finance Act 1986. It is understood that HMRC regards the facilities of the Depositary Trust Company as a clearance service for these purposes and that no relevant election under Section 97A of the UK Finance Act 1986 has been made.

Transfers of our ordinary shares within a clearance service where an election has been made by the clearance service under Section 97A of the UK Finance Act 1986 will generally be subject to SDRT (rather than stamp duty) at the rate of 0.5% of the amount or value of the consideration.

Transfers of our ordinary shares that are held in certificated form will generally be subject to UK stamp duty at the rate of 0.5% of the consideration given (rounded up to the nearest £5). An exemption from UK stamp duty is available for a written instrument transferring an interest in our 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 for which the aggregate consideration exceeds £1,000. SDRT may be payable on an agreement to transfer such ordinary shares, generally at the rate of 0.5% of the consideration given in money or money's worth under the agreement to transfer the ordinary shares. This charge to SDRT would be discharged if an instrument of transfer is executed pursuant to the agreement which gave rise to SDRT and UK stamp duty is duly paid on the instrument transferring the ordinary shares within six years of the date on which the agreement was made or, if the agreement was conditional, the date on which the agreement became unconditional.

If our ordinary shares (or interests therein) are subsequently transferred into a clearance service or depositary receipt system, UK stamp duty or SDRT will generally be payable at the rate of 1.5% of the amount or value of the consideration given or, in certain circumstances, the value of the shares (save to the extent that an election has been made under Section 97A of the UK Finance Act 1986). This liability for UK stamp duty or SDRT will strictly be accountable by the clearance service or depositary receipt system, as the case may be, but will, in practice, generally be reimbursed by participants in the clearance service or depositary receipt system.

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;

- 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,
- 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 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.

Underwriter	Number of Ordinary Shares
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.

	Per Ordinary Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

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,

- 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 Prospective 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.

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,

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 the ordinary shares offered hereby will be passed upon for us by Latham & Watkins LLP with respect to certain legal matters of the United States federal securities, New York State and English law. 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 England and Wales. We have been advised that there is some doubt as to the enforceability in the United Kingdom, 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 United Kingdom. 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 United Kingdom 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 United Kingdom do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

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*.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS
MEIRAGTX LIMITED AND SUBSIDIARIES
FOR THE YEARS ENDED DECEMBER 31, 2016 AND 2017

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 and in accordance with auditing standards generally accepted in the United States of America. 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 auditors since 2016

Stamford, Connecticut
March 29, 2018

MEIRAGTX LIMITED AND SUBSIDIARIES
CONSOLIDATED BALANCE SHEETS

	December 31, 2016	December 31, 2017
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 17,476,641	$ 8,548,638
Prepaid expenses	1,212,183	1,961,243
Other current assets	400,956	965,233
Total Current Assets	19,089,780	11,475,114
Property and equipment, net	3,016,525	14,255,729
Restricted cash	444,844	123,376
TOTAL ASSETS	$ 22,551,149	$ 25,854,219
LIABILITIES, CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' DEFICIT		
CURRENT LIABILITIES:		
Accounts payable	$ 1,474,213	$ 7,055,380
Accrued expenses	4,018,103	9,332,944
Note payable	—	1,442,009
Warrant liability	—	2,679,633
Capitalized lease obligation—current portion	6,015	30,850
Due to Kadmon	543,038	861,030
Total Current Liabilities	6,041,369	21,401,846
Capitalized lease obligation	5,458	34,298
Deferred rent	588,491	266,290
Other liabilities	221,254	178,419
TOTAL LIABILITIES	6,856,572	21,880,853
COMMITMENTS		
CONVERTIBLE PREFERRED C SHARES		
Convertible Preferred C Shares, $0.00001 nominal value, 6,111,526 and 19,428,037 issued and outstanding at December 31, 2016 and 2017, respectively (liquidation preference of $33,002,240 and $52,455,700 at December 31, 2016 and 2017, respectively)	32,833,660	51,338,631
SHAREHOLDERS' DEFICIT:		
A Ordinary Shares, $0.00001 nominal value 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	342	342
Capital in excess of nominal value	17,900,995	20,080,713
Accumulated other comprehensive loss	(661,112)	(2,022,477)
Accumulated deficit	(34,379,308)	(65,423,843)
Total Shareholders' Deficit	(17,139,083)	(47,365,265)
TOTAL LIABILITIES, CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' DEFICIT	$ 22,551,149	$ 25,854,219

See Notes to Consolidated Financial Statements

MEIRAGTX LIMITED AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	For the Year Ended December 31,	
	2016	2017
Operating expenses:		
General and administrative	$ 6,026,529	$ 9,325,017
Research and development	14,037,918	22,359,712
Total operating expenses	20,064,447	31,684,729
Loss from operations	(20,064,447)	(31,684,729)
Other non-operating income (expense)		
Foreign currency gain	265,543	1,676,117
Convertible note inducement expense	—	(553,500)
Change in fair value of warrant liability	—	(465,633)
Interest income	32,068	26,073
Interest expense	(25,440)	(42,863)
Net loss	(19,792,276)	(31,044,535)
Net loss attributable to the non-controlling interest in subsidiary	305,883	—
Net loss attributable to MeiraGTx shareholders	(19,486,393)	(31,044,535)
Other comprehensive loss	(671,391)	(1,361,365)
Comprehensive loss	(20,157,784)	(32,405,900)
Less: comprehensive loss (income) attributable to non-controlling interest	8,520	—
Comprehensive loss attributable to MeiraGTx shareholders	$ (20,149,264)	$ (32,405,900)
Net loss attributable to MeiraGTx shareholders	$ (19,486,393)	$ (31,044,535)
Accretion on convertible preferred C shares	(85,425)	(806,963)
Adjusted net loss attributable to MeiraGTx ordinary shareholders	$ (19,571,818)	$ (31,851,498)
Basic and diluted net loss per ordinary share attributable to ordinary shareholders	$ (0.63)	$ (0.96)
Weighted-average number of ordinary shares outstanding—basic and diluted	31,098,591	33,269,157

See Notes to Consolidated Financial Statements

MEIRAGTX LIMITED AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' DEFICIT
AS OF DECEMBER 31, 2017

	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
Issuance of convertible preferred C shares in connection with restructuring	6,149,326	—	—	—	—	—	—	—	—	—
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	—	191,963	—	—	—	(191,963)	—	—	—	(191,963)
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)

See Notes to Consolidated Financial Statements

MEIRAGTX LIMITED AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS

	For the Year Ended December 31,	
	2016	**2017**
Cash flows from operating activities:		
Net loss	$ (19,792,276)	$ (31,044,535)
Adjustments to reconcile net loss to net cash used in operating activities:		
Issuance of shares for services	443,136	17,000
Share-based compensation expense	2,806,961	2,959,731
Foreign currency gain	(261,817)	(1,676,117)
Depreciation	243,081	679,177
Amortization of interest on asset retirement obligation	17,248	19,313
Change in fair value of warrant liability	—	465,633
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
(Increase) decrease in operating assets:		
Prepaid expenses and other current assets	(960,993)	(669,756)
Other current assets	(302,901)	(493,424)
Restricted cash	(441,049)	321,468
Increase (decrease) in operating liabilities:		
Accounts payable	453,130	4,728,491
Accrued expenses	1,333,796	4,969,619
Due to Kadmon	800,223	317,992
Deferred rent	255,160	(324,019)
Net cash used in operating activities	(14,809,001)	(17,733,918)
Cash flows from investing activities:		
Purchase of property and equipment	(2,593,584)	(10,535,717)
Net cash used in investing activities	(2,593,584)	(10,535,717)
Cash flows from financing activities:		
Payments on capitalized lease obligation	(5,480)	(24,388)
Proceeds from the issuance of note payable	—	2,500,000
Proceeds from the issuance of ordinary and convertible preferred C shares and warrants, net of issuance costs	20,762,682	16,854,653
Proceeds from exercised stock options	—	9,950
Net cash provided by financing activities	20,757,202	19,340,215
Net increase (decrease) in cash and cash equivalents	3,354,617	(8,929,420)
Effect of exchange rate changes on cash	(421,240)	1,417
Cash and cash equivalents at beginning of year	14,543,264	17,476,641
Cash and cash equivalents at end of year	$ 17,476,641	$ 8,548,638
Supplemental disclosure of non-cash transactions:		
Fixed asset acquisition included in accounts payable and accrued expenses at end of year	$ 301,655	$ 415,650
Conversion of note payable into convertible preferred C shares	$ —	$ 2,500,000
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)
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ —	$ 20,894

See 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 amyothrophic 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 preclinical 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 5, 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 totaled $65,423,843, 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 fund its expenses into the fourth quarter of 2018.

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.

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 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, and MeiraGTx UK Limited ("Meira UK"), a limited company under the laws of England and Wales. The consolidated financial statements also include the accounts of MeiraGTx UK II Limited, which was a 60% owned subsidiary from April 27, 2015 through April 8, 2016. On April 8, 2016, the Company acquired the remaining 40% interest in MeiraGTx UK II.

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

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 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. The Company evaluated all events and transactions through March 29, 2018, the date these consolidated financial statements were issued. 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 statement of operations and comprehensive loss. These warrants 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 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 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 shows the values of the Company's financial assets and liabilities that are required to be measured at fair value on a recurring basis:

		Fair Value Measurement Using:		
Description	December 31, 2016	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Restricted cash	$ 444,844	$ 444,844	$ —	$ —
Total	$ 444,844	$ 444,844	$ —	$ —

		Fair Value Measurement Using:		
Description	December 31, 2017	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Restricted cash	$ 123,376	$ 123,376	$ —	$ —
Warrants	2,679,633	—	—	2,679,633
Total	$ 2,803,009	$ 123,376	$ —	$ 2,679,633

The table below shows 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 December 31, 2017:

	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

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:

	September 21, 2017	November 2, 2017	December 31, 2017
Risk-free interest rate	1.38%	1.53%	1.72%
Expected volatility	80%	80%	80%
Expected dividend yield	0	0	0
Expected life	18 months	18 months	9 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 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, except in the event of a change of control which is outside the control of the Company and requires shareholder approval. The redemption value of the Preferred Shares upon a change in control is equal to its liquidation value described below.

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:

Asset Category	Useful Lives
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 2016 or 2017.

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 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.

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 Company funded outside research programs, 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, (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 and $1.45 per share as of December 31, 2016, September 15, 2017 and December 31, 2017, 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 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 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.

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.

The change in asset retirement obligations is as follows:

	For the year ended December 31,	
	2016	2017
Balance at beginning of year	$ —	$ 221,254
Inception of asset retirement obligation	205,659	—
Amortization of interest	17,248	19,313
Change in estimate	—	(75,011)
Effects of exchange rate	(1,653)	12,863
Balance at end of year	$ 221,254	$ 178,419

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' deficit 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:

	December 31, 2016	December 31, 2017
United States	$ 1,081,522	$ 436,463
United Kingdom	2,379,847	13,942,642
	$ 3,461,369	$ 14,379,105

Accounting Pronouncements Recently Adopted

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 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 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 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 Company does not expect that the adoption of ASU 2017-01 will have a material effect on its financial position, results of operations or cash flows.

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 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 will be 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. The Company currently presents changes in restricted cash as an operating activity in the statement of cash flows. Upon adoption of ASU 2016-18, such changes will be reflected in the beginning and ending balances of cash, cash equivalents and restricted cash for all periods presented.

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 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 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 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, 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 Company does not believe that ASU 2014-09 will have a material impact on its consolidated financial statements. but could impact the Company's

significant accounting policies if the Company were to generate revenue in 2018 and adopt ASU 2014-09 in 2018.

In February 2016, the FASB issued ASU No. 2016-01, *Leases (Topic 842)*, or ASU 2016-01, 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 preclinical 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).

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 and December 31, 2017, 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 at December 31, 2016 and 2017 consist of the following:

	December 31, 2016	December 31, 2017
Research and Development	$ 418,483	$ 624,348
Clinical Trial Costs	204,028	497,869
Clinical Trial Materials	—	341,775
Dues and License Fees	49,487	145,594
Insurance	144,525	163,284
Rent	214,764	27,778
Other	180,896	160,595
	$ 1,212,183	$ 1,961,243

5. Property & Equipment, net:

Property and equipment, net at December 31, 2016 and 2017 consist of the following:

	December 31, 2016	December 31, 2017
Leasehold Improvements	$ 2,203,282	$ 10,873,895
Manufacturing Equipment	—	2,477,637
Laboratory Equipment	662,443	993,409
Office Equipment	100,350	276,100
Asset Retirement Obligation	205,659	153,133
Furniture & Fixtures	78,708	93,786
	3,250,442	14,867,960
Less: Accumulated depreciation	(233,917)	(612,231)
	$ 3,016,525	$ 14,255,729

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.

Capitalized leases in the amount of $17,817 and $95,880 are included in office equipment at December 31, 2016 and 2017, respectively, and accumulated depreciation of $6,928 and 34,552 at December 31, 2016 and 2017, respectively

Depreciation expense was $243,081 and $679,177 for the years ended December 31, 2016 and 2017 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, 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 and $123,376 of restricted cash included in long-term assets as of December 31, 2016 and 2017, respectively and is measured using level 1 inputs.

7. Accrued Expenses:

Accrued expenses at December 31, 2016 and 2017 were comprised of the following:

	December 31, 2016	December 31, 2017
Clinical Trial Costs	$ 664,149	$ 4,859,410
Compensation and Benefits	1,418,958	2,386,903
Consulting	1,158,915	1,220,477
Rent	242,937	387,267
Professional Fees	323,102	231,923
Interest	—	33,437
Other	210,042	213,527
	$ 4,018,103	$ 9,332,944

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:

	December 31, 2016	December 31, 2017
2018	$ 6,834	$ 34,410
2019	5,695	28,715
2020	—	7,179
Total minimum lease payments	12,529	70,304
Less: amount representing interest	(1,056)	(5,156)
Present value of net minimum lease payments	11,473	65,148
Less: current portion	(6,015)	(30,850)
Obligations under capital lease, less current portion	$ 5,458	$ 34,298

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 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. 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 for the year ended December 31, 2017.

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.

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 is as follows:

	Number of Options	Weighted-Average Exercise Price	Aggregate Instrinsic Value
Outstanding at December 31, 2015	—	$ —	$ —
Granted	1,295,000	1.99	
Exercised	—	—	
Expired	—	—	
Forfeited	—	—	
Outstanding at December 31, 2016	1,295,000	$ 1.99	$ —
Granted	2,375,000	0.96	
Exercised	(5,000)	(1.95)	
Expired	—	—	
Forfeited	(22,000)	(1.99)	
Outstanding at December 31, 2017	3,643,000	$ 1.32	$ 1,420,650
Weighted average remaining contractual life of options outstanding as of December 31, 2016 (yrs)	9.19		
Weighted average remaining contractual life of options outstanding as of December 31, 2017 (yrs)	9.09		
Options exercisable at December 31, 2016	125,000	$ 1.99	$ —
Options exercisable at December 31, 2017	723,398	$ 1.99	$ —
Weighted average remaining contractual life of options exercisable as of December 31, 2016 (yrs)	9.24		
Weighted average remaining contractual life of options exercisable as of December 31, 2017 (yrs)	8.21		

The total fair value of options vested during the years ended December 31, 2016 and 2017 was $180,723 and $898,699, respectively.

During the years ended December 31, 2016 and 2017, the Company granted 915,000 and 1,020,000 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):

	2016	2017
Risk-free interest rate	1.38% - 1.55%	2.28%
Expected volatility	90%	90%
Expected dividend yield	0%	0%
Expected life of employee and Board of Directors' options (in years)	5.0 - 6.1	5.5 - 6.1

As of December 31, 2016 and 2017, 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 and $987,413, respectively which is expected to be realized over a period of 3.17 and 3.42 years, respectively. The Company will issue shares upon exercise of options from Ordinary Shares reserved.

During the years ended December 31, 2016 and 2017, the Company granted 380,000 and 1,355,000 share options, respectively to non-employee consultants. In accordance with ASC 505-50, on December 31, 2016 and 2017, 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:

	2016	2017
Risk-free interest rate	2.45%	2.36% - 2.39%
Expected volatility	90%	90%
Expected dividend yield	0%	0%
Expected life of non-employee options (in years)	9.2 - 10.0	8.2 - 9.7

As of December 31, 2016 and 2017, the total compensation expense relating to unvested options granted to non-employee consultants that had not yet been recognized was $456,707 and $1,629,019, respectively, which is expected to be realized over a period of 3.17 and 3.72 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 was $1.51 and $0.80, 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 as of the respective dates of issuance, and are included in loss from operations over the requisite service period.

A summary of the restricted Ordinary Shares is as follows:

	Ordinary Shares	$ Value
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

During the years ended December 31, 2016 and 2017 the Company recognized total share-based compensation expense in the accompanying statements of operations and comprehensive loss as follows:

	2016	2017
Research and development	$ 1,995,594	$ 2,374,899
General and administrative	811,367	584,832
Total share based compensation	$ 2,806,961	$ 2,959,731

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.

11. Convertible Preferred C Shares and Shareholders' Deficit:

Registration Rights Related to Ordinary Shares and Preferred Shares

Holders of 3% or more of the Company's fully diluted shares and certain shareholders have piggyback registration rights with respect to the Company's registration of its ordinary shares. The shareholders' agreement, including these registration rights, terminate upon an initial public offering.

Ordinary Shares

Voting Rights

Each share is entitled to one vote.

Redemption

The shares are not redeemable.

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.

Pre-Emptive Rights

The holders of the Ordinary Shares have the right to participate in any new offering of equity shares, subject to certain exceptions including a qualified IPO in which either (i) the listing of any or all of the shares on a regulated market (pursuant to the Markets in Financial Instruments Directive), including without limitation the New York Stock Exchange and NASDAQ National Market, where such listing raises a minimum amount of $40,000,000 or, with the prior written consent of a majority of the holders of Series C preferred shares only, less than $40,000,000 or (ii) the acquisition of the Company by an acquirer who is listed on a regulated market and whereby pursuant to the acquisition the acquirer is required to prepare a prospectus, Form S-1 or equivalent admission document, or Qualified IPO.

Drag-Along Rights

Pursuant to the Company's articles of association if the holders of more than 51% of the Ordinary Shares wish to sell their Ordinary Shares, then the drag members have the right to require all other holders to accept the offer made to the drag members and sell their Ordinary Shares on the same terms, subject to certain exceptions with respect to the Company's registration of its Ordinary Shares.

Tag-Along Rights

Pursuant to the Company's articles of association if Kadmon holds more than 15% of the fully diluted Ordinary Shares and proposes to transfer more than 25% of the aggregate number of Ordinary Shares held by Kadmon 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, subject to certain exceptions with respect to the Company's registration of its Ordinary Shares.

Right to Appointment Board Member

Pursuant to the shareholders' agreement, as long as Kadmon's ownership percentage of the Company is in excess of 10%, Kadmon has the right to appoint a board member to the Company's board of directors. 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 1.

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.

Convertible Preferred C Shares

Redemption

The Preferred Shares are not redeemable, except in the event of a change of control which is outside the control of the Company and requires shareholder approval. The redemption value of the Preferred Shares upon a change in control is equal to its liquidation value described below.

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 the subscription price received by the Company in respect of such shares;
- second, in paying to the holders of Ordinary Shares a sum equal to the nominal amount of each share held by them; and
- third, 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 extinguishment and concurrent dividend resulted in $91,203 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 the completion of a Qualified IPO.

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.

Drag-Along Rights

If the holders of more than 51% of the Preferred Shares wishes to sell their Preferred Shares, then the drag members have the right to require all other holders to accept the offer made to the drag members and sell their shares on the same terms.

Tag-Along Rights

If one or more of the holders of the Preferred Shares 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 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, it shall have the right to appoint a board member to the Company's board of directors, which it did on October 19, 2017.

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.

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).

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-Sholes 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, which resulted in an increase of the warrant liability in the amount of $465,633, 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 was $2,679,633.

12. Net Loss per Share

The Company computes net loss per share in accordance with ASC 260-10, *Earnings per Share* (see Note 2).

Basic and diluted net loss per share is computed as follows:

	2016	2017
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	$ (19,571,818)	$ (31,851,498)
Weighted-average ordinary shares outstanding:		
Basic and Diluted	31,098,591	33,269,157
Net loss per share:		
Basic and Diluted	$ (0.63)	$ (0.96)

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:

	December 31, 2016	December 31, 2017
Preferred Shares	6,111,256	19,428,037
Restricted Ordinary Shares subject to forfeiture	1,489,333	411,049
Share options	1,295,000	3,643,000
Warrants	—	3,600,000
	8,895,589	27,082,086

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.

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:

	December 31, 2016	December 31, 2017
United Kingdom	$ (17,285,861)	$ (26,458,625)
United States	(2,506,415)	(4,585,910)
	$ (19,792,276)	$ (31,044,535)

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:

	December 31, 2016		December 31, 2017	
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 U.K. rate change (17% at expected DTA turn)	582,910	-2.95%	482,350	-1.55%
U.S. Federal & State Rate Change (Jobs Act & MTA)	—	0.00%	993,999	-3.20%
Change in valuation allowance	3,516,208	-17.76%	4,942,855	-15.92%
Actual income tax benefit effective tax rate	$ 0	0.00%	$ 0	0.00%

The Expense/(Benefit) for income taxes from continuing operations consists of the following:

	December 31, 2016	December 31, 2017
Current Tax Expense/(Benefit)		
United Kingdom	$ —	$ —
United States	—	—
Total Current	—	—
Deferred Tax Expense/(Benefit)		
United Kingdom	(2,034,368)	(3,759,109)
United States	(1,481,840)	(1,183,746)
Total Deferred	(3,516,208)	(4,942,855)
Change in Valuation Allowance	3,516,208	4,942,855
Total Income Tax Expense/(Benefit)	$ —	$ —

Deferred Tax Assets

	December 31, 2016		
	Total	UK	US
Deferred Tax Assets:			
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	5,756,250	3,303,159	2,453,091
Less: valuation allowance	(5,756,250)	(3,303,159)	(2,453,091)
Net deferred tax asset	$ —	$ —	$ —

	December 31, 2017		
	Total	UK	US
Deferred Tax Assets:			
Net operating loss carryforwards	$ 9,462,691	$ 6,909,754	$ 2,552,937
Other	539,008	152,554	386,454
R&D Credit	697,406	—	697,406
Deferred tax assets	10,699,105	7,062,308	3,636,797
Less: valuation allowance	(10,699,105)	(7,062,308)	(3,636,797)
Net deferred tax asset	$ —	$ —	$ —

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 is it more likely than not that these assets will not be fully realized.

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 30-days' notice.

During the years ended December 31, 2016 and 2017, the Company incurred the following charges in connection with the TSA and is included in loss from operations:

	2016	2017
Rent	$ 794,087	$ 548,229
Personnel	189,104	39,721
Other	42,110	5,983
Total charges incurred	$ 1,025,301	$ 593,933

During the year ended December 31, 2016 and 2017, the Company made cash payments totaling $225,078 and $275,941, 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 is $543,038 and $861,030, 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 was approximately $278,000 and $538,000, respectively. Future obligations, under the agreement equal £1,058,303, or approximately $1,438,869 through October 2020.

The amount due to UCL under the master services agreement at December 31, 2016 and 2017 is $251,754 and $775,315, respectively and is included in accounts payable and accrued expenses on the balance sheet.

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 was approximately $456,106 and $1,904,352, respectively.

The amount due to UCL under the manufacturing and drug supply agreement at December 31, 2016 and 2017 is $412,395 and $2,466,142, 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, the balance of deferred rent, representing the difference between cash rent paid and straight-line rent expense, was $243,780 and $231,276, respectively.

Total rent expense under this operating lease was $243,780 and $487,559 for the years ended December 31, 2016 and 2017, respectively. As of December 31, 2017, the aggregate future minimum rental payments under this lease are $2,181,520.

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, the balance of deferred lease obligation, representing the difference between cash rent paid and straight-line rent expense, was $11,380 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, respectively. Aggregate future minimum rental payments under this lease are $332,442.

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.

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, the Company recorded $17,247 and $7,571 of interest expense, respectively. The carrying value of the asset retirement obligation at December 31, 2016 and 2017 is $221,254 and $178,419, respectively. Total rent expense under this operating lease was $266,698 and $279,303 for the years ended December 31, 2016 and 2017, 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.

In June 2017, the Company entered into two non-cancellable operating leases, expiring in July 2018, for office facilities in London, U.K. 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, the balance of deferred lease obligation, representing the difference between cash rent paid and straight-line rent expense, was $35,014. Total rent expense under theses operating leases was $0 and $85,222 for the years ended December 31, 2016 and 2017, respectively.

The aggregate future minimum rental payments under these leases are as follows:

2018	$365,713
2019	$293,130
2020	$293,130
2021	$ 24,427
Total future rent payments	$976,400

The aggregate future minimum rental payments of all leases, including those discussed in Note 14 are as follows:

2018	$1,215,723
2019	$ 828,813
2020	$ 847,562
2021	$ 598,264
Total future rent payments	$3,490,362

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 by either party at any time upon twelve months' written 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. Future obligations to be paid under these agreements equal £110,000, or approximately $150,000, using exchange rates as of December 31, 2017.

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 restricted Ordinary Shares. 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 $850,000. 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.

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 $1,912,500, as of December 31, 2017.

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.

Effective January 1, 2016, the Company entered into a one-year consulting agreement, which has been extended annually through December 31, 2018, with an entity controlled by former chairman of the board. The agreement provides for an annual consulting fee of $400,000 and a discretionary bonus as determined by the Company's compensation committee. For the years ended December 31, 2016 and 2017, the Company recorded $850,000 and $850,000, respectively, in research and development costs in connection with the agreement.

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. Future obligations to be paid under the CRADA, as amended, through March 25, 2021 equal $276,250.

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 were $325,343 and $418,000, respectively. Future obligations to be paid under the agreement through March 22, 2019 equal $418,000.

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 were $63,337 and $1,029,904, respectively. Future obligations to be paid under the agreement through December 5, 2019 equal $3,273,179.

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 were $0 and $698,307, 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 10th 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 were $67,775 and $73,250, 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 were $0 and $82,260, respectively.

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 $4,500,000, 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. 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, employer contributions to all plans were $128,281 and $252,700, respectively.

17. Subsequent Events:

Management has evaluated subsequent events through March 29, 2018, the date these financial statements were issued. Based on our evaluation, the following disclosures have been made:

Preferred Shares

From January 1, 2018 through March 29, 2018, the Company issued 16,943,396 Preferred Shares at an offering price of $2.70 per share for gross proceeds in the amount of $45,747,173.

Issuance of A Shares

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 (see Note 15). Additionally, under the terms of the employment agreements, the Company was required to pay the income taxes on those shares. Compensation expense in the amount of $6,154,608 will be recorded during the quarter ended March 31, 2018.

Option Grants

On January 10, 2018, the Company granted 1,125,000 share options to certain officers of the Company. The options have a strike price of $1.45 per share, with 25% vesting on the first anniversary date of grant and the balance vesting ratably over the next 36 months. The fair market value of the share options of $1.09 per share were calculated using the Black-Scholes valuation model.

Also, on January 10, 2018, the Company also granted 425,000 share options to the non-employee directors of the Company. The options have an exercise price of $1.45 per share and vest on the one-year anniversary of the date of grant. The fair market value of the share options of $1.05 per share were calculated using the Black-Scholes valuation model.

Shares

Ordinary Shares

P R O S P E C T U S

BofA Merrill Lynch

Barclays

Evercore ISI

Chardan

, 2018

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.

	Amount
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	$ *

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

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 29, 2018, the registrant issued an aggregate 36,389,760 Series A ordinary shares for an aggregate consideration of approximately $8.7 million.

From October 1, 2015 through March 29, 2018, the registrant issued an aggregate 36,423,285 Series C preferred shares for an aggregate consideration of approximately $97.9 million.

(b) Equity Grants.

From March 4, 2016 through January 10, 2018, the registrant granted stock options to purchase an aggregate of 5,149,750 Series A ordinary shares with exercise prices ranging between $0.68 and $1.99 per share to employees, non-employee consultants, and directors from the early exercise of stock options in connection with services provided to the registrant by such parties.

(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) 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) 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 associated 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.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

Exhibit Number	Description of Exhibit
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
5.1*	Opinion of Latham & Watkins LLP
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*	Lease Agreement, dated December 15, 2016, between MieraGTx Limited and ARE-East River Science Park LLC
10.6*	Lease Agreement, dated February 2, 2016, between MieraGTx Limited and Moorfields Eye Hospital NHS Foundation Trust and Kadmon Corporation LLC
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 MieraGTx Limited and Richard Giroux

Exhibit Number	Description of Exhibit
10.9*	Employment Agreement, dated April 27, 2015, between MeiraGTx Limited and Stuart Naylor, Ph.D.
10.10*†	License Agreement, dated May 1, 2013 between MeiraGTx Limited, Brandeis University and BRI-Alzan Inc., as amended.
10.11*†	License Agreement, dated February 4, 2015 between Athena Vision Ltd. and UCL Business, Plc, as amended.
10.12*†	License Agreement, dated July 28, 2017 between MeiraGTx Limited and UCL Business, Plc, as amended.
10.13*†	License Agreement between MeiraGTx Limited, Meira GTx UKII-Limited and UCL Business Plc, dated as of March 15, 2018.
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Ernst & Young LLP
23.2*	Consent of Latham & Watkins LLP (included in Exhibit 5.1)
24.1*	Power of Attorney (included on signature page)

* 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 day of , 2018.

MeiraGTx Holdings plc

By: _____
Alexandria Forbes, Ph.D.
President and Chief Executive Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of MeiraGTx Holdings plc., hereby severally constitute and appoint Alexandria Forbes, Ph.D. and , 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.

Signature	Title	Date
_____ Alexandria Forbes, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	, 2018
_____ Keith R. Harris, Ph.D.	Director	, 2018
_____ Arnold J. Levine, Ph.D.	Director	, 2018
_____ Ellen Hukkelhoven, Ph.D.	Director	, 2018
_____ Joel S. Marcus	Director	, 2018
_____ Neil Mendoza	Director	, 2018
_____ Stuart Naylor, Ph.D.	Director	, 2018
_____ Thomas E. Shenk, Ph.D.	Director	, 2018