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As filed with the Securities and Exchange Commission on June 4, 2018.

**Registration No. 333-224914**

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

# AMENDMENT NO. 3
# TO
# FORM S-1
# REGISTRATION STATEMENT
**UNDER**
**THE SECURITIES ACT OF 1933**

# MeiraGTx Holdings plc
(Exact name of registrant as specified in its charter)

| Cayman Islands | 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.**
**MeiraGTx LLC**
**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.** ☐

**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)(4) |
|---|---|---|
| Ordinary shares, $0.00003881 nominal value per share | $92,000,000 | $11,454 |

**(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)** The Registrant previously paid the registration fee in full.
**(4)** 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.**

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Subject to Completion
Preliminary Prospectus dated June 4, 2018.

**PROSPECTUS**

# 5,000,000 Shares

MEIRAGTx

## Ordinary Shares

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This is MeiraGTx Holdings plc's initial public offering. We are offering 5,000,000 of our ordinary shares.

We expect the initial public offering price to be between $14.00 and $16.00 per ordinary share. Currently, no public market exists for our ordinary shares. Our ordinary shares have been approved for listing on the Nasdaq Global Select 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 13 of this prospectus.**

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

(1) We refer you to "Underwriting" beginning on page 207 for additional information regarding underwriting compensation.

The underwriters may also exercise their option to purchase up to an additional 750,000 ordinary shares from us, at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus.

Certain of our existing shareholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount and commissions on these shares as they will on any other shares sold to the public in this offering.

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.

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*Joint Book-Running Managers*

**BofA Merrill Lynch** **Barclays** **Evercore ISI**

*Lead Manager*

**Chardan**

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The date of this prospectus is , 2018.

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

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

## ABOUT THIS PROSPECTUS

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

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

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

## PROSPECTUS SUMMARY

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

### Overview

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

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

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;

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

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

| Product Candidate | Indication | Development Stage | | | Status |
|---|---|---|---|---|---|
| | | Preclinical | Phase 1/2 | Phase 3 | |
| **Ophthalmology Programs** | | | | | |
| AAV-CNGB3 | **Achromatopsia** (*CNGB3*) | Orphan U.S. & EU; RPDD; PRIME[1,2,3,4] | | | • Phase 1/2 ongoing |
| AAV-CNGA3 | **Achromatopsia** (*CNGA3*) | | | | • Phase 1/2 expected initiation in 2019 |
| AAV-RPGR | **X-linked RP** (*RPGR*) | Orphan U.S. & EU; Fast Track Designation[1,2,5] | | | • Phase 1/2 ongoing |
| AAV-RPE65 | ***RPE65*-Deficiency** (*RPE65*) | Orphan U.S. & EU; RPDD[1,2,3] | | | • Phase 1/2 ongoing |
| A006 | **Wet AMD** (*anti-VEGFR2*) | | | | • First in man clinical trials expected 2019 |
| **Salivary Gland Programs** | | | | | |
| AAV-AQP1 | **Xerostomia** (*hAQP1*) | Orphan U.S.[1] | | | • Phase 1 ongoing |
| AAV-AQP1 | **Sjogren's** (*hAQP1*) | | | | • Phase 1/2 expected initiation in 2019 |
| **Neurodegenerative Diseases Program** | | | | | |
| AAV-UPF1 | **ALS** (*UPF1*) | | | | • First in man clinical trials expected 2019 |

1. Orphan drug designation by the FDA.
2. Orphan drug designation by European Medicines Agency, or the EMA.
3. Rare pediatric disease designation by Offices of Orphan Products Development and Pediatric Therapeutics of the FDA.
4. Priority medicines, or PRIME, designation by the EMA.
5. Fast Track designation by the FDA.

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

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

**Our Ophthalmology Programs**

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

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

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

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

**Our Salivary Gland Programs**

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

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

**Our Neurodegenerative Disease Programs**

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

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

**Our Strengths**

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

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

- **Potentially Transformative Gene Regulation Technology Platform:** We are developing proprietary technology for innovative gene therapy treatments whose expression can be turned on and off with an easily administered small molecule. We believe the capacity for temporal control of gene therapy products has the potential to transform the gene therapy landscape by opening up new treatment possibilities.

- **Manufacturing Capabilities and Capacity:** We have a flexible and scalable cGMP manufacturing facility and production process, which we expect can supply all of our current clinical and preclinical programs through regulatory approval and, should they be approved, provide sufficient capacity for their commercial production.

- **Robust and Diverse Clinical and Preclinical Pipeline:** Applying our portfolio approach to gene therapy product development, our initial focus is on treatments for IRDs, salivary glands disorders and neurodegenerative diseases with potential for accelerated approval and has produced four ongoing clinical programs and multiple preclinical development programs.

- **Relationships with Leading Institutions:** Our longstanding relationships with leading institutions and experts provides us with guidance on development strategy and access to potential patients for our clinical trials.

- **Natural History Study Data:** We sponsor ongoing prospective long-term natural history studies in IRDs that facilitate our ability to efficiently enroll our treatment studies, potentially reducing clinical trial timelines and providing insight into the appropriate endpoints for regulatory approval.

**Our Strategy**

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

- successfully complete clinical development, obtain regulatory approval and commercialize our pipeline of gene therapy product candidates to treat disorders of the eye and salivary gland;

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

- utilize our viral vector design and optimization capabilities to identify and develop new gene therapies for other serious diseases;

- advance the development of our potentially transformative proprietary technology for regulating the activity of gene therapy products using small molecules and initiate clinical trials of new product candidates; and

- evaluate strategic collaborations with other biotechnology and pharmaceutical companies to leverage our capabilities, manufacturing capacity and proprietary gene regulation technology.

**Risk Factors**

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

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

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

**Implications of Being an Emerging Growth Company**

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

- being permitted to present only two years of audited financial statements and only two years of related Management’s Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;

- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and

- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

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

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

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

**Corporate Information**

MeiraGTx Holdings plc was formed on May 1, 2018 under the laws of the Cayman Islands. The registered office of the Company is situated at the offices of Walkers Corporate Limited, Cayman Corporate Centre, 27 Hospital Road, George Town, Grand Cayman KY1-9008, Cayman Islands. MeiraGTx Limited, a private company formed under the laws of England and Wales, is a subsidiary of MeiraGTx Holdings plc and will be its predecessor accounting entity upon closing of the offering. 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**

Following the effectiveness of this registration statement and prior to the start of trading of our ordinary shares on the Nasdaq Global Select Market, we will effect a corporate reorganization, pursuant to which the outstanding shares of MeiraGTx Limited will be exchanged for equivalent shares of MeiraGTx Holdings plc. MeiraGTx Holdings plc will become the direct parent of MeiraGTx Limited and the holding company of the business and will be the issuer of ordinary shares in this offering. We refer to these events in this prospectus as the "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 financial statements of MeiraGTx Limited and its consolidated subsidiaries will present the results of operations of MeiraGTx Holdings plc and its consolidated subsidiaries.

Following the Corporation Reorganization and prior to the start of trading of our ordinary shares on the Nasdaq Global Select Market, we also expect to effect a 1 for 3.881 reverse share split (by way of consolidation of the share capital of the Company) on all outstanding ordinary shares and preferred shares of MeiraGTx Holdings plc. Prior to the closing of the offering, the preferred shares of MeiraGTx Holdings plc, and the preferred shares issued as a result of the exercise of all outstanding warrants, will convert into A ordinary shares and all A ordinary shares (including those resulting from the conversion of our preferred shares) shall be re-designated as ordinary shares.

**Indications of Interest**

Certain of our existing shareholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount and commissions on these shares as they will on any other shares sold to the public in this offering.

## The Offering

| | |
|---|---|
| Ordinary shares offered by us | 5,000,000 ordinary shares. |
| Ordinary shares to be outstanding after this offering | 27,184,140 ordinary shares (or 27,934,140 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 750,000 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 $67.0 million (or approximately $77.5 million if the underwriters exercise their option to purchase additional ordinary shares in full), based on an assumed initial public offering price of $15.00 per ordinary share, after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us. We anticipate that we will use the net proceeds of this offering to continue to develop our most advanced product candidates, AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, scale-up our manufacturing facility and related processes, fund research and development of other pipeline product candidates and technologies, and the remainder, if any, to fund new and ongoing research and development activities and for working capital and other general corporate purposes as set forth under "Use of Proceeds" beginning on page 73. |
| 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 Select Market symbol | "MGTX" |

The number of our ordinary shares to be outstanding after this offering is based on 9,376,360 ordinary shares outstanding as of April 30, 2018, including 22,777 unvested restricted shares subject to repurchase, and excludes:

- 1,614,346 ordinary shares issuable upon exercise of share options outstanding under our 2016 Equity Incentive Plan, referred to as our 2016 Plan, as of April 30, 2018, at a weighted-average exercise price of $5.32 per ordinary share;
- 3,054,996 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; and
- 509,166 ordinary shares reserved for future issuance under our 2018 Employee Share Purchase Plan, referred to as our 2018 ESPP, 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 ESPP.

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

- the Corporate Reorganization;
- other than in the consolidated financial statements and related notes thereto included elsewhere in this prospectus or as otherwise indicated, a 1 for 3.881 reverse share split of all outstanding ordinary shares and preferred shares (by way of consolidation of the share capital of the Company), which will be effective following the Corporate Reorganization and prior to the start of trading of the ordinary shares on the Nasdaq Global Select Market;
- the exercise of all outstanding warrants by the holders thereof for an aggregate of 927,594 preferred shares for an aggregate purchase price of $9.7 million;
- the conversion of all of our preferred shares, including 927,594 preferred shares that will be issued as a result of the exercise of all outstanding warrants, into an aggregate of 11,501,432 ordinary shares prior to the closing of this offering;
- the issuance to Alexandria Forbes, Ph.D., our President and Chief Executive Officer, and Rich Giroux, our Chief Operating Officer of an aggregate of 1,306,348 ordinary shares, which number of shares assumes that we sell the number of shares set forth on the cover page of this prospectus in this offering, on the date the registration statement of which this prospectus forms a part becomes effective or, if later, on the date we file a registration statement on Form S-8 covering the issuance of the ordinary shares. 435,450 of these ordinary shares vest immediately and 870,898 will vest in eight equal quarterly installments beginning three months after effectiveness of this registration statement. These grants are referred to in this prospectus as the “Executive IPO Grants”;
- no exercise of outstanding options after April 30, 2018; and
- no exercise by the underwriters of their option to purchase additional ordinary shares in this offering.

Certain of our existing shareholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount and commissions on these shares as they will on any other shares sold to the public in this offering.

**Summary Consolidated Financial Data**

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

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

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

(1) See Note 12 to our consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical basic and diluted net loss per ordinary share and the weighted-average number of shares used in the computation of the per share amounts. Shares outstanding does not give effect to the anticipated 1 for 3.881 reverse stock split (by way of consolidation of the share capital of the Company) described elsewhere in this prospectus.

| | As of March 31, 2018 | | |
|---|---|---|---|
| | Actual | Pro Forma(1) | Pro Forma As Adjusted(2)(3) |
| **Consolidated Balance Sheet Data:** | | | |
| Cash and cash equivalents | $ 32,356,851 | $54,464,388 | $ 121,464,388 |
| Total assets | $ 50,780,903 | $72,888,440 | $ 139,888,440 |
| Total liabilities | $ 14,345,189 | $12,334,964 | $ 18,866,714 |
| Convertible preferred C shares | $ 97,351,080 | — | — |
| Total shareholders’ (deficit) equity | $(60,915,366) | $60,553,476 | $ 121,021,741 |

(1) The pro forma data above gives effect to (a) the Corporate Reorganization described under “Summary—Corporate Reorganization”, (b) the conversion of all outstanding preferred shares, including preferred shares issued in connection with the exercise of warrants for cash in an amount equal to $9.7 million, into ordinary shares prior to the closing of this offering, (c) the reclassification of the related warrant liability into capital in excess of nominal value, and (d) our issuance of 4.7 million preferred shares in April 2018 for aggregate proceeds of $12.7 million.

(2) The pro forma as adjusted data above reflects (a) the pro forma adjustments described in footnote (1) above, (b) the issuance of the Executive IPO Grants plus the accrual of expenses in the amount of $6.5 million, based on an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, related to our obligation to pay associated income taxes incurred by the named executive officers in connection therewith (such $6.5 million amount representing only one-third of our total obligation to pay income taxes incurred by the named executive officers upon vesting of the Executive IPO Grants, based on an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus) and (c) the issuance and sale of 5,000,000 ordinary shares in this offering at an assumed initial public offering price of $15.00 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 $15.00 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 $4.6 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 $13.9 million, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us.

## RISK FACTORS

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

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

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

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

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

Before we generate any revenue from product sales, each of our programs and product candidates will require additional preclinical and/or clinical development, potential regulatory approval in multiple jurisdictions, manufacturing, building of a commercial organization, substantial investment and significant marketing efforts. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or FDA, European Medicines Agency, or EMA, or other regulatory authorities to perform preclinical studies and clinical trials in addition to those that we currently anticipate. These risks are further described under "—Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval" and "—Risks Related to Commercialization." As a result, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our shareholders' equity and working capital.

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

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

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

Our operations have consumed significant amounts of cash since inception. As of March 31, 2018, our cash and cash equivalents were $32.4 million. Based 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 the third quarter of 2020. 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-RPGR, AAV-RPE65 and AAV-AQP1, which are still in development, and if none of them receive regulatory approval or are successfully commercialized, our business may be harmed.***

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The clinical trials and manufacturing of our product candidates are, and the manufacturing and marketing of our products, if approved, will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and market our product candidates. Before obtaining regulatory approvals for the commercial sale of any of our product 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. In the device compatibility assay, the FDA noted a disparity between the target titer for the intended low dose dilution and the actual titer obtained on polymerase chain reaction, or PCR, analysis. The FDA requested clarification on whether this was an imprecise dilution scheme for the low dose or a PCR assay issue. We submitted our second response to the FDA on May 2, 2018 providing data that identified the issue as a PCR assay artifact and also showing data that we believe supports that this has now been addressed. On May 31, 2018 the FDA released the clinical hold on our IND for AAV-CNGB3.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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. Additionally, on May 11, 2018, President Trump laid out his administration's "Blueprint" to reduce the cost of prescription drugs while preserving innovation and cures. The Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. Although some of these, and other, proposals 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-RPGR, AAV-RPE65 and AAV-AQP1, if approved, for certain markets overseas; however, we cannot assure that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that they will have effective sales forces.

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

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

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

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

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

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

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

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

The ACA includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor’s own pre-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have an adverse effect on the future commercial prospects for our biological products.

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

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

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

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

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

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

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

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

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

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

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

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

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

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

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

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

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

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

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

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

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

Misconduct by our employees and independent contractors, including consultants, vendors, and any third parties we may engage in connection with development and commercialization, could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, EMA and other similar regulatory authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

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

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

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

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

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

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

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

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

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

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

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

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

Prior to this offering, there has been no public market for our ordinary shares. Although we have been approved to list our ordinary shares on The Nasdaq Global Select 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 April 30, 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 53.0% of our outstanding ordinary shares. In addition, based on the number of ordinary shares outstanding as of April 30, 2018, Kadmon Corporation, LLC owned 16.9% of our outstanding ordinary shares before this offering and is expected to own ordinary shares representing approximately 13.0% of our outstanding voting shares upon the closing of this offering.

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.

Certain of our existing stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The foregoing discussion does not reflect any potential purchases by these potential purchasers. See "Principal Shareholders" for more information regarding the ownership of our outstanding ordinary shares by our executive officers, directors and their affiliates.

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

The initial public offering price of our ordinary shares will be substantially higher than the net tangible book value per share of our ordinary shares. Therefore, if you purchase our ordinary shares in this offering, you 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 $15.00 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 $11.06 per share as of March 31, 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 27.0% of the aggregate price paid by all purchasers of our ordinary shares but will own only approximately 18.4% of our ordinary shares outstanding after this offering.

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

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

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

Sales of a substantial number of our ordinary shares in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our ordinary shares. After this offering, we will have outstanding 27,184,140 ordinary shares (or 27,934,140 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. Substantially all of the remaining 22,184,140 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 16,123,234 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 4,669,342 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.

Certain of our existing shareholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share. Any such shares purchased by shareholders who are considered to be our affiliates cannot be resold in the public market immediately following this offering as a result of restrictions under securities laws, but will be able to be sold following the expiration of these restrictions as described in the “Shares Eligible for Future Sale.”

***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.

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

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

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

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

In particular, investors should be aware that there is uncertainty as to whether the courts of the Cayman Islands or any other applicable jurisdictions would recognize and enforce judgments of U.S. courts obtained against us or our directors or management as well as against the selling shareholders predicated upon the civil liability provisions of the securities laws of the United States or any state in the United States or entertain original actions brought in the Cayman Islands or any other applicable jurisdictions courts against us or our directors or officers as well as against the selling shareholders predicated upon the securities laws of the United States or any state in the United States.

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

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

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

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

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

We expect our first Section 404(a) assessment will take place for our annual report for the fiscal year ending December 31, 2019. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inadequate internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our ordinary shares.

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

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

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

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

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

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

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

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

Based on the current and anticipated value of our assets, including goodwill, and the composition of our income, assets and operations, we do not believe we were a "passive foreign investment company," or PFIC, for the taxable year ending on December 31, 2017, and do not expect to be a PFIC for the current taxable year. However, the application of the PFIC rules is subject to uncertainty in several respects, and we cannot assure you that the U.S. Internal Revenue Service, or the IRS, will not take a contrary position. Furthermore, a separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. Accordingly, we cannot assure you that we were not a PFIC for our taxable year ending on December 31, 2017 and that we will not be a PFIC for our current taxable year or any future taxable year. A non-U.S. company will be considered a PFIC for any taxable year if (i) at least 75% of its gross income is passive income (including interest income), or (ii) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income. If we were to be classified as a PFIC for any taxable year during which a U.S. Holder (as defined below under "Material U.S. Federal Income Tax Consequences") holds our ordinary shares, certain adverse U.S. federal income tax consequences could apply to such U.S. Holder, including (i) the treatment of all or a portion of any gain on disposition of our ordinary shares as ordinary income, (ii) the application of a deferred interest charge on such gain and the receipt of certain dividends and (iii) the obligation to comply with certain reporting requirements. See "Material U.S. Federal Income Tax Consequences—Passive Foreign Investment Company Rules."

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

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

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

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

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

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

In October 2015, the Organization for Economic Co-Operation and Development released a final package of measures to be implemented by member nations in response to a 2013 action plan calling for a coordinated multi-jurisdictional approach to “base erosion and profit shifting” by multinational companies. Multiple member jurisdictions, including the countries in which we operate, have begun implementing recommended changes such as country-by-country reporting requirements and changes to double tax treaties. Additional multilateral changes are anticipated in upcoming years. We often rely on generally available interpretations of applicable tax laws, treaties and regulations. There cannot be certainty that the relevant tax authorities are in agreement with our interpretation of these laws, regulations or treaties, or with tax positions that we have taken. If our interpretation or tax position is challenged by the relevant tax authorities, we could be required to pay taxes that we currently do not collect or pay, may be subject to interest and penalties and there could be an increase to the costs of our services to track and collect such taxes, which could increase our costs of operations or our effective tax rate. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a “permanent establishment” under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. The occurrence of any of the foregoing tax risks could have a material adverse effect on our business, financial condition and results of operations.

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

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

As of December 31, 2017, we had federal and state NOL carryforwards in the United States of $7.8 million and $7.8 million, respectively, and cumulative carryforward tax losses in the United Kingdom of $40.0 million, which we expect to be available to reduce future taxable income subject to any relevant restrictions (including those in the UK that limit the percentage of profits that can be reduced by carried forward losses). The U.S. federal and state NOL carry forwards will begin to expire in 2035 and the U.K. carryforward tax losses will continue indefinitely, subject to relevant restrictions, under current UK legislation. Also, as of December 31, 2017, we had research and development credits in the U.S. in the amount of $697,000.

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

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

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

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

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

## INDUSTRY AND OTHER DATA

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

## USE OF PROCEEDS

We estimate that the net proceeds to us from our issuance and sale of our ordinary shares in this offering will be approximately $67.0 million, assuming an initial public offering price of $15.00 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 $77.5 million. Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per ordinary share would increase (decrease) the net proceeds to us from this offering by approximately $4.6 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 $13.9 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, together with cash and cash equivalents of $32.4 million as of March 31, 2018, for the following purposes:

- approximately $20 million to $25 million to further develop our most advanced product candidates, AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1 through completion of Phase 1/2 trials;

- approximately $10 million to $15 million to scale up our manufacturing facility and related processes;

- approximately $10 million to $15 million to fund research and development of our other pipeline product candidates and technologies; and

- the remainder, if any, to fund pivotal trials for AAV-CNGB3, AAV-CNGA3, AAV-RPGR and AAV-RPE65, 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 the third quarter of 2020. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources.

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

## DIVIDEND POLICY

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

## CAPITALIZATION

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

- on an actual basis reflecting the capitalization of MeiraGTx Limited;

- on a pro forma basis to reflect (a) the Corporation Reorganization described under "Summary—Corporate Reorganization", (b) the conversion of all outstanding preferred shares, including preferred shares issued in connection with the exercise of warrants for cash in an amount equal to $9.7 million, into ordinary shares prior to the closing of this offering, (c) the reclassification of the related warrant liability into capital in excess of nominal value, and (d) our issuance of 4.7 million preferred shares in April 2018 for aggregate proceeds of $12.7 million; and

- on a pro forma as adjusted basis to give further effect to (a) the issuance of 1,306,348 ordinary shares (435,450 shares of which will vest upon closing of the offering), which reflects the Executive IPO Grants, plus the accrual of expenses in the amount of $6.5 million, based on an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, related to our obligation to pay associated income taxes incurred by the named executive officers in connection therewith (such $6.5 million amount representing only one-third of our total obligation to pay income taxes incurred by the named executive officers upon vesting of the Executive IPO Grants, based on an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus) and (b) our issuance and sale of 5,000,000 ordinary shares in this offering at an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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

| | As of March 31, 2018 | | |
|---|---|---|---|
| | Actual, MeiraGTx Limited | Pro Forma, MeiraGTx Holdings plc | Pro Forma As Adjusted, MeiraGTx Holdings plc(1) |
| Cash and cash equivalents | $ 32,356,851 | $ 54,464,388 | $ 121,464,388 |
| Warrant liability | $ 2,010,225 | $ — | $ — |
| Series C preferred shares, $0.00001 nominal value per share; 9,361,141 shares issued and outstanding, actual; no shares, issued and outstanding, pro forma and pro forma as adjusted | 97,351,080 | — | — |
| Shareholders' (deficit) equity: | | | |
| Ordinary shares, $0.00003881 nominal value per share; 9,336,540 shares issued and outstanding, actual; 20,877,792 shares issued and outstanding, pro forma; 27,184,140 shares issued and 26,313,242 shares outstanding, pro forma as adjusted | 364 | 810 | 1,055 |
| Capital in excess of nominal value | 23,691,708 | 145,336,087 | 218,867,607 |
| Accumulated other comprehensive loss | (2,780,242) | (2,780,242) | (2,780,242) |
| Accumulated deficit | (81,827,196) | (82,003,179) | (95,066,679) |
| Total shareholders' (deficit) equity | (60,915,366) | 60,553,476 | 121,021,741 |
| Total capitalization | $ 36,435,714 | $ 60,553,476 | $ 121,021,741 |

(1) Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 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 $4.6 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 $13.9 million.

The number of shares in the table above includes 37,270 unvested restricted shares and does not include:

- 1,614,346 ordinary shares issuable upon exercise of share options outstanding under our 2016 Plan as of March 31, 2018, at a weighted-average exercise price of $5.32 per ordinary share;
- 3,054,996 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; and
- 509,166 ordinary shares reserved for future issuance under our 2018 ESPP, 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 ESPP.

# DILUTION

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

As of March 31, 2018, we had a historical net tangible book value of $22.4 million, or $2.40 per ordinary share. Our historical net tangible book value per share represents total tangible assets less total liabilities, divided by the number of our ordinary shares outstanding as of March 31, 2018.

Our pro forma net tangible book value as of March 31, 2018 was $46.6 million, or $2.23 per ordinary share. Pro forma net tangible book value represents the amount of our total tangible assets less total liabilities, after giving effect to (a) the Corporate Reorganization described under "Summary—Corporate Reorganization", (b) the conversion of all outstanding preferred shares, including preferred shares issued in connection with the exercise of warrants for cash in an amount equal to $9.7 million, into ordinary shares prior to the closing of this offering, (c) the reclassification of the related warrant liability into capital in excess of nominal value, and (d) our issuance of 4.7 million preferred shares in April 2018 for aggregate proceeds of $12.7 million. Pro forma net tangible book value per ordinary share represents our pro forma net tangible book value divided by the total number of ordinary shares outstanding as of March 31, 2018, after giving effect to the pro forma adjustment described above.

After giving further effect to (a) the issuance of the Executive IPO Grants plus the accrual of expenses in the amount of $6.5 million, based on an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, related to our obligation to pay associated income taxes incurred by the named executive officers (such $6.5 million amount representing only one-third of our total obligation to pay income taxes incurred by the named executive officers upon vesting of the Executive IPO Grants, based on an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus) and (b) receipt of the net proceeds from our issuance and the sale of 5,000,000 ordinary shares in this offering at an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2018 would have been approximately $107.1 million, or approximately $3.94 per ordinary share. This amount represents an immediate increase in pro forma net tangible book value of $1.71 per ordinary share to our existing shareholders and an immediate dilution of approximately $11.06 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 | | $15.00 |
| Historical net tangible book value per ordinary share as of March 31, 2018 | $ 2.40 | |
| Decrease per ordinary share attributable to the conversion of our preferred shares | (0.17) | |
| Pro forma net tangible book value per ordinary share as of March 31, 2018 | 2.23 | |
| Increase per ordinary share attributable to this offering | 1.71 | |
| Pro forma as adjusted net tangible book value per ordinary share after this offering | | 3.94 |
| Dilution per ordinary share to new investors in this offering | | $11.06 |

Each $1.00 increase (decrease) in the assumed initial public offering price of $15.00 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 $0.17, and dilution in pro forma net tangible book value per ordinary share to new investors by $0.17, 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 $0.36 per ordinary share and decrease the dilution to new investors by $0.36 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 $0.39 per ordinary share and increase the dilution to new investors by $0.39 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 $4.21 per ordinary share, the increase in pro forma net tangible book value per ordinary share would be $0.30 and the dilution per share to new investors would be $10.79 per ordinary share, in each case assuming an initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us.

The following table summarizes the pro forma as adjusted basis described above, as of March 31, 2018, the differences between the number of ordinary shares purchased from us, the total consideration paid to us in cash and the average price per share that existing shareholders and new investors paid. The calculation below is based on an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

| | Shares Purchased | | Total Consideration | | Average Price |
|---|---|---|---|---|---|
| | Number | Percent | Number | Percent | Per Share |
| Existing shareholders | 22,184,140 | 81.6% | $128,742,388 | 63.2% | $ 5.80 |
| New investors | 5,000,000 | 18.4 | 75,000,000 | 36.8 | $ 15.00 |
| Total | 27,184,140 | 100.0% | $203,742,388 | 100.0% | |

Certain of our existing shareholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The table above does not reflect any potential purchases by these potential purchasers.

The foregoing tables and calculations are based on the number of our ordinary shares outstanding as of March 31, 2018 (which included 37,270 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:

- 1,614,346 ordinary shares issuable upon exercise of share options outstanding under our 2016 Plan as of March 31, 2018, at a weighted-average exercise price of $5.32 per share;
- 3,054,996 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; and

- 509,166 ordinary shares reserved for future issuance under our 2018 ESPP, 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 ESPP.

To the extent any of these outstanding options is exercised, there will be further dilution to new investors. If all of such outstanding options had been exercised as of March 31, 2018, the pro forma as adjusted net tangible book value per ordinary share after this offering would be $4.01, and total dilution per ordinary share to new investors would be $10.99.

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 79.4% of the total number of our ordinary shares outstanding after this offering; and

- the number of shares held by new investors will increase to 5,750,000, or approximately 20.6% of the total number of our ordinary shares outstanding after this offering.

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## SELECTED CONSOLIDATED FINANCIAL DATA

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

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

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

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

(1) See Note 12 to our consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical basic and diluted net loss per ordinary share and the weighted-average number of shares used in the computation of the per share amounts. Shares outstanding does not give effect to the anticipated 1 for 3.881 reverse share split (by way of consolidation of the share capital of the Company) described elsewhere in this prospectus.

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

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

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

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

### Overview

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

We are a private limited company incorporated under the laws of England and Wales, and were formed and commenced operations in 2015. Our discussion of our financial condition and results of operations is based upon our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. Since our formation, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facility and developing manufacturing processes, advancing the product candidates in our ophthalmology, salivary gland and neurodegenerative disease programs, building our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, and providing general and administrative support for these operations. In 2016, we completed the acquisition of assets held by BRI-Alzan, Inc., a Delaware corporation, including a worldwide license agreement to develop certain preclinical technology for the treatment of ALS. To date, we have financed our operations primarily with cash on hand and proceeds from the sales of our Series C preferred shares and Series A ordinary shares. Through March 31, 2018, we received gross proceeds of approximately $97.6 million from sales of our Series C preferred shares. In addition, from April 1, 2018 through April 30, 2018, we issued 1,212,697 Series C preferred shares for gross proceeds of $12.7 million. As of April 30, 2018, we had cash and cash equivalents of $39.8 million.

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

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

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

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 the third quarter of 2020. 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, | | | Three Months Ended March 31, | | |
|---|---|---|---|---|---|---|
| | 2016 | 2017 | Change | 2017 | 2018 | Change |
| Ophthalmology programs | $ 2,026,592 | $ 4,133,015 | $2,106,423 | $ 766,505 | $1,465,179 | $ 698,674 |
| Salivary gland programs | 967,745 | 913,706 | (54,039) | 225,101 | 211,215 | (13,886) |
| Neurodegenerative diseases programs | 922,127 | 2,220,843 | 1,298,716 | 425,737 | 604,518 | 178,781 |
| Manufacturing | 379,656 | 3,213,861 | 2,834,205 | 275,868 | 792,387 | 516,519 |
| Other research and development costs | 9,741,798 | 11,878,287 | 2,136,489 | 3,130,144 | 3,854,023 | 723,879 |
| Total research and development expenses | $14,037,918 | $22,359,712 | $8,321,794 | $4,823,355 | $6,927,322 | $2,103,967 |

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

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

***Foreign Currencies***

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

***Income Taxes***

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

***Research and Development***

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

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

***Share-Based Compensation***

*Options*

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

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

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

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

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

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 $7.57, $2.64, $5.63 and $6.02 per share as of December 31, 2016, September 15, 2017, December 31, 2017 and March 31, 2018, respectively.

The decrease in the valuation from December 31, 2016 to September 15, 2017 was due primarily to the Company decreasing the offering price of the Series C preferred shares from $20.96 per share at December 31, 2016 to $10.48 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. However in the event of a Sale (as defined in the Articles of Association), which would include a change of control that is outside of our control, the Series C preferred shares are entitled to receive a payment which is equal to their liquidation value. The feature is being accounted for as a redemption under ASC 480.

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

**Results of Operations**

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

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

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

*General and Administrative Expenses*

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

*Research and Development Expenses*

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

*Foreign Currency Gain*

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

*Change in Fair Market Value of Warrant Liability*

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

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

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

| | Year Ended December 31, 2016 | Year Ended December 31, 2017 | Change |
|---|---|---|---|
| Operating expenses: | | | |
| General and administrative | $ 6,026,529 | $ 9,325,017 | $ 3,298,488 |
| Research and development | 14,037,918 | 22,359,712 | 8,321,794 |
| Total operating expenses | 20,064,447 | 31,684,729 | 11,620,282 |
| Loss from operations | (20,064,447) | (31,684,729) | (11,620,282) |
| Other non-operating income (expense): | | | |
| Foreign currency gain | 265,543 | 1,676,117 | 1,410,574 |
| Convertible note inducement expense | — | (553,500) | (553,500) |
| Change in fair value of warrant liability | — | (465,633) | (465,633) |
| Interest income | 32,068 | 26,073 | (5,995) |
| Interest expense | (25,440) | (42,863) | (17,423) |
| Net loss | $ (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 million was primarily due to a weakening U.S. dollar against the pound sterling in 2017.

*Convertible Note Inducement Expense*

There was no convertible note inducement expense for the year ended December 31, 2016 compared to $0.5 million for the year ended December 31, 2017. The increase of $0.5 million was primarily due to the issuance of a warrant to purchase 231,898 Series C preferred shares in 2017 to a convertible noteholder as an inducement to convert the note into Series C preferred shares.

*Change in Fair Market Value of Warrant Liability*

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

***Liquidity and Capital Resources***

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

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

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

***Cash Flows***

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

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

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

*Operating Activities*

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

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

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

During the year ended December 31, 2017, our cash used in operating activities of $18.1 million was primarily due to our net loss of $31.0 million as we incurred expenses associated with research activities on our clinical programs and research activities for our other product candidates and incurred general and administrative expenses. The loss included non-cash charges of $3.0 million, which consisted of $3.0 million of share-based compensation, change in fair value of warrant liability in the amount of $0.5 million, convertible note inducement expense of $0.5 million and depreciation of $0.7 million, which was partially offset by a foreign currency gain of $1.7 million. Additionally, current liabilities, consisting of accounts payable, accrued expenses deferred rent and due to affiliate, increased by $11.1 million, was partially offset by decreases in current assets, consisting of prepaid expenses and other current assets, in the amount of $1.2 million.

*Investing Activities*

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

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

*Financing Activities*

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

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

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

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

***Funding Requirements***

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

Specifically, our expenses will increase as we:

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

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 the third quarter of 2020. 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 four ongoing clinical programs and a broad pipeline of preclinical and research programs. We have core capabilities in viral vector design and optimization and gene therapy manufacturing, as well as a potentially transformative gene regulation technology. Led by an experienced management team, we have taken a portfolio approach by licensing, acquiring and developing technologies that give us depth across both product candidates and indications. Though initially focusing on the eye, salivary gland and central nervous system, we intend to expand our focus in the future to develop additional gene therapy treatments for patients suffering from a range of serious diseases.

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

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.

| Product Candidate | Indication | Development Stage | | | Status |
|---|---|---|---|---|---|
| | | 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 ongoing |
| AAV-CNGA3 | **Achromatopsia** *(CNGA3)* | | | | • Phase 1/2 expected initiation in 2019 |
| AAV-RPGR | **X-linked RP** *(RPGR)* | Orphan U.S. & EU; Fast Track Designation[1,2,5] | | | • Phase 1/2 ongoing |
| AAV-RPE65 | ***RPE65*-Deficiency** *(RPE65)* | Orphan U.S. & EU; RPDD[1,2,3] | | | • Phase 1/2 ongoing |
| A006 | **Wet AMD** *(anti-VEGFR2)* | | | | • First in man clinical trials expected 2019 |
| **Salivary Gland Programs** | | | | | |
| AAV-AQP1 | **Xerostomia** *(hAQP1)* | Orphan U.S.[1] | | | • Phase 1 ongoing |
| AAV-AQP1 | **Sjogren's** *(hAQP1)* | | | | • Phase 1/2 expected initiation in 2019 |
| **Neurodegenerative Diseases Program** | | | | | |
| AAV-UPF1 | **ALS** *(UPF1)* | | | | • First in man clinical trials expected 2019 |

1. Orphan drug designation by the FDA.
2. Orphan drug designation by European Medicines Agency, or the EMA.
3. Rare pediatric disease designation by Offices of Orphan Products Development and Pediatric Therapeutics of the FDA.
4. Priority medicines, or PRIME, designation by the EMA.
5. Fast Track designation by the FDA.

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

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

- geographic atrophy age related macular degeneration, or dry AMD – use of gene therapy technology to introduce light sensitive molecules into rod photoreceptors in order to restore some aspects of vision lost in this disease;

- amyotrophic lateral sclerosis, or ALS—targeting dysregulation of neuronal RNA processing, which we believe may lead to the degeneration of motor neurons that occurs in ALS;

- Alzheimer's disease—targeting endosomal trafficking, which is a central mechanism that we believe underlies Alzheimer's disease; and

- gene regulation—use of our proprietary RNA shape regulation cassette to switch gene therapy product candidates on and off with small molecules, potentially transforming gene therapy technology into a delivery mechanism for a broad array of biologic drugs.

***Our Ophthalmology Programs***

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

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

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

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

***Our Salivary Gland Programs***

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

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

***Our Neurodegenerative Disease Programs***

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

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

**Our Strengths**

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

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

- **Potentially Transformative Gene Regulation Technology Platform:** We are developing proprietary technology to enable innovative gene therapy treatments whose expression can be turned on and off with an easily administered small molecule. We believe the capacity for temporal control of gene therapy products has the potential to transform the gene therapy landscape by opening up new treatment possibilities.

- **Manufacturing Capabilities and Capacity:** We have a flexible and scalable cGMP manufacturing facility and production process, which we expect can supply all of our current clinical and preclinical programs through regulatory approval and, should they be approved, provide sufficient capacity for their commercial production.

- **Robust and Diverse Clinical and Preclinical Pipeline:** Applying our portfolio approach to gene therapy product development, our initial focus is on treatments for IRDs, salivary glands disorders and neurodegenerative diseases with potential for accelerated approval and has produced four ongoing clinical programs and multiple preclinical development programs.

- **Relationships with Leading Institutions:** Our longstanding relationships with leading institutions and experts provides us with guidance on development strategy and access to potential patients for our clinical trials.

- **Natural History Study Data:** We sponsor ongoing prospective long-term natural history studies in IRDs that facilitate our ability to efficiently enroll our treatment studies, potentially reducing clinical trial timelines and providing insight into the appropriate endpoints for regulatory approval.

### Our Strategy

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

- successfully complete clinical development, obtain regulatory approval and commercialize our pipeline of gene therapy product candidates to treat disorders of the eye and salivary gland;

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

- utilize our viral vector design and optimization capabilities to identify and develop new gene therapies for other serious diseases;

- advance the development of our potentially transformative proprietary technology for regulating the activity of gene therapy products using small molecules and initiate clinical trials of new product candidates; and

- evaluate strategic collaborations with other biotechnology and pharmaceutical companies to leverage our capabilities, manufacturing capacity and proprietary gene regulation technology.

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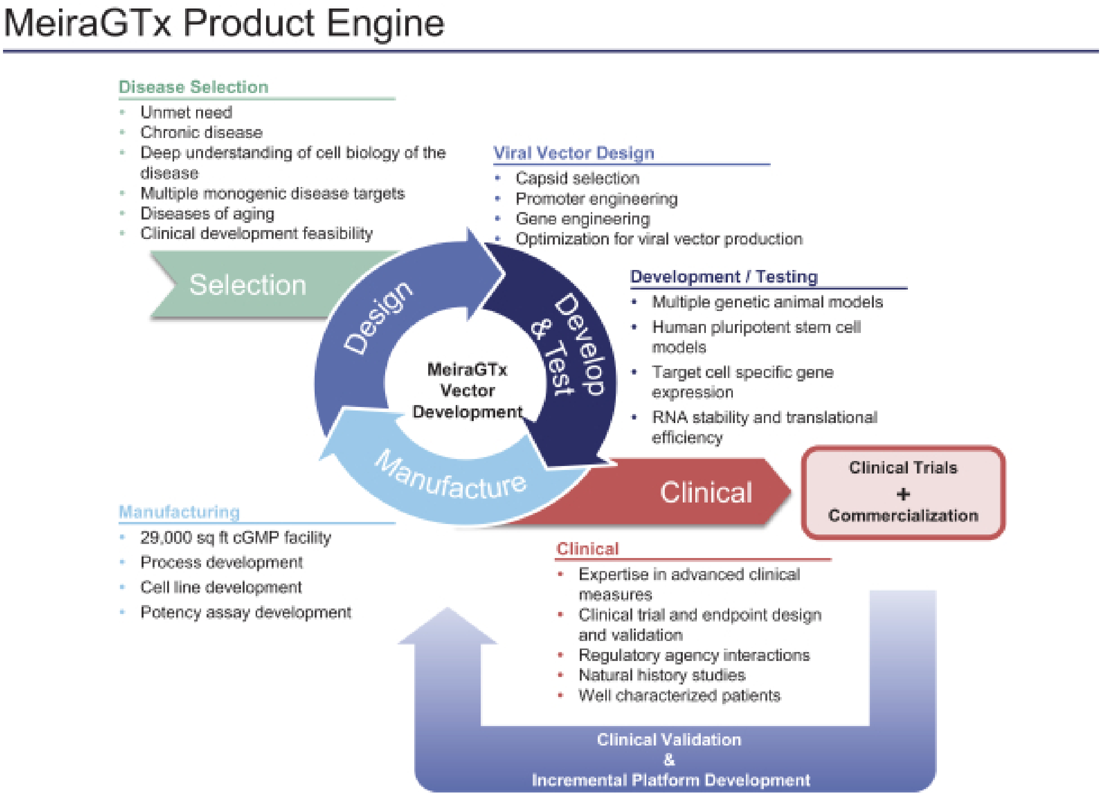
The figure below depicts the steps in our product engine, including disease selection, design, development/testing, clinical and manufacturing:




**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 neurodegenerative diseases, including ALS and Alzheimer's disease.

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

**Our Ophthalmology Programs**

***Overview and Strategy***

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

- The eye is easily accessible and has highly compartmentalized anatomy, which allows for accurate delivery of vectors to specific tissues using direct visualization and microsurgical techniques.

- The structure of the eye allows for efficient delivery to specific cell subtypes with small volumes of vector, making the dose per patient much lower than for systemic treatment.

- Anatomical barriers and unique structure of the eye make the immune response to the intraocular administration of vectors more attenuated than systemic administration.

- Largely non-dividing cell populations in the eye make good targets for potentially stable, long-term gene delivery and expression.

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

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

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

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

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

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

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

IRDs as a class are the most common cause of blindness in the working age population worldwide and a leading cause of impaired vision in children in developed countries. There are approximately 200,000 people in each of the United States and European Union affected by IRDs. However, IRDs may be caused by mutations in over 200 identified genes, and in many cases each genetically defined IRD may be a small patient population. Meaningful clinical trials for these sorts of rare indications are especially challenging because they require access to sufficient patients and baseline data on each patient in order to secure clear indicators of efficacy as a result of intervention. We seek to address this problem by sponsoring prospectively designed natural history studies in each of the indications that we are treating in our Phase 1/2 trials.

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

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

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

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

***Achromatopsia***

*Disease Background and Market Opportunity*

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

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

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

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

*Our Gene Therapy Program*

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

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

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

*ACHM Caused By Mutations in CNGB3*

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

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

Preclinical studies in mice lacking the *Cngb3* gene were carried out by our collaborators at UCL IO and led by Professor Robin Ali in 2010 and 2011 and the data was published in *Human Molecular Genetics* in 2011. In these studies, it was observed that delivery of our *CNGB3* product candidate, AAV-CNGB3, via subretinal injection at doses between 6E$^{9}$ and 8E$^{9}$ viral genomes per eye, or vg/eye, was associated with a restoration of cone function to near normal levels.

In one of these studies, retinal response to light was measured in three groups of mice: *Cngb3* mutant mice treated with AAV-CNGB3, untreated *Cngb3* mutant mice and normal mice. Mice were treated with AAV-CNGB3 vector dosed at 2E$^{12}$ vg/mL (8E$^{9}$ vg/eye) via subretinal injection. One eye was treated per mouse. Vector was administered when mice were 30 days old, and electrical responses, or ERGs, of the retina were measured 90 days following administration of the vector.

Figure 1 shows representative ERG responses of the retina to different light stimuli: a single flash of bright light (1A; 1B; 1C) and repeated pulses, or flickers, of bright light at different frequencies to assess the refresh rate of the photoreceptors (1A'; 1B'; 1C'). Retinas from three different groups of mice were tested: retinas of normal mice (Figure 1A), retinas of mutant mice lacking the *Cngb3* gene (Figure 1B) and retinas of mutant mice lacking the *Cngb3* gene, but treated with AAV-CNGB3 (Figure 1C). It was observed that the response to a bright light pulse was largely absent in the retinas of *Cngb3* mutant mice, as this response is largely mediated by the cones and is therefore severely impacted by the *Cngb3* mutation (Figure 1B). It was also observed that treatment of *Cngb3* mutant mice with AAV-CNGB3 was associated with a high-degree of restored cone function in these mutant mouse retinas in response to a single flash of bright light (Figure 1C). In addition, we tested the response of cones to rapid flickers of bright light (Figure 1A') because only cones can register multiple sequential signals from rapid flickers. It was observed that registering rapid flickers was also impacted by the *Cngb3* mutation (Figure 1B') and the cone flicker response was nearly completely restored in the retinas of *Cngb3* mutant mice following treatment with AAV-CNGB3 (Figure 1C').

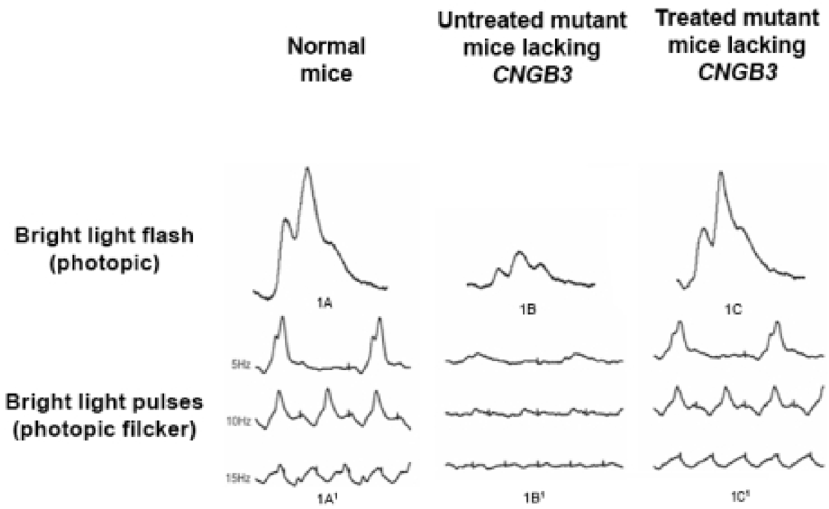


**Figure 1.** Electrical responses of the retina reacting to two different light stimuli: a single flash of bright light and repeat pulses of bright light at increasing frequency, or flickers.

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

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

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

In another one of the preclinical studies carried out by our collaborators at UCL IO, it was assessed whether functional improvement at the retinal level of *Cngb3* mutant mice was impacted by the age of the mice at the time treatment with the gene therapy product candidate. In this study, *Cngb3*-mutant mice were treated with AAV-CNGB3 at 30 days old, the P30 group, or 180 days old, the P180 group. One eye was treated in each mouse via subretinal injection dosed at 2E12 vg/mL (8E9 vg/eye). Optomotor measurements were taken 60 days after treatment of the P30 group of the *Cngb3* mutant mice treated with AAV-CNGB3 (n=11), untreated *Cngb3* mutant mice (n=11) and normal, age-matched untreated mice (n=5). Optomotor measurements were also taken 60 days after the treatment of the P180 group of the *Cngb3* mutant mice treated with AAV-CNGB3 (n=6), untreated *Cngb3* mutant mice (n=6) and normal, age-matched untreated mice (n=5). Optomoter assessments were made by placing each mouse on a pedestal located in the center of four inward facing computer screens, that projected a rotating image. The head-tracking responses of each mouse was observed using an overhead infrared video camera. Visual acuity was measured by involuntary reflex head-tracking responses driven by the left (clockwise rotations, black arrow) and right (counter-clockwise rotations, white arrow) eyes, respectively (Figure 2A).

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

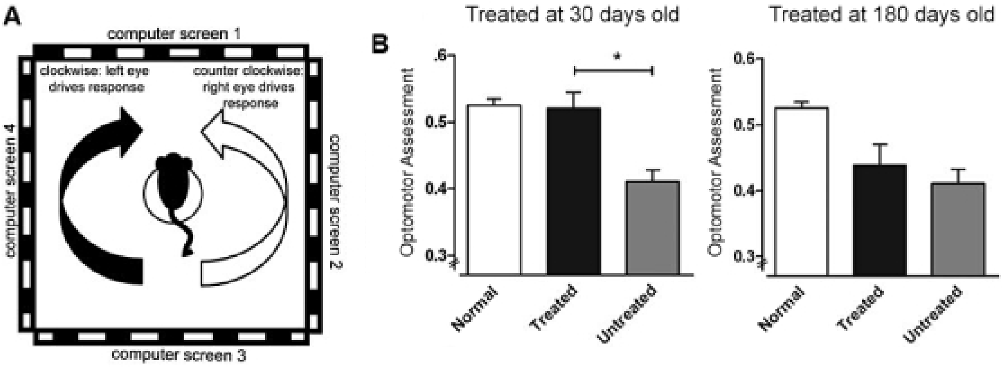



**Figure 2A.** Depiction of how optomotor assessments were taken. Each mouse was placed on a pedestal located in the center of four inward facing screens and was observed by an overhead infrared video camera. The assessments were made 60 days following treatment of the *Cngb3* mutant mice with AAV-CNGB3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

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

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

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

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

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

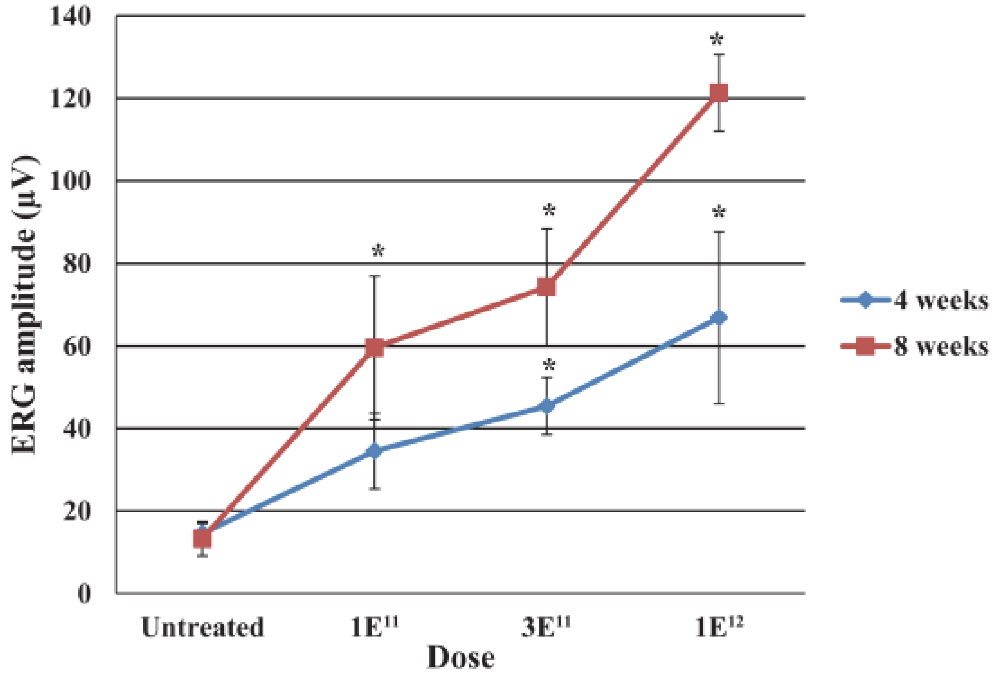



**Figure 3.** Graph of averaged photopic ERG amplitudes at four and eight week time-points post administration of AAV-CNGB in *Cngb3* mutant mice treated at four weeks of age. The blue line indicates the electrical response amplitudes observed following administration of different doses of AAV-CNGB3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

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

*Clinical Development of AAV-CNGB3*

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

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

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

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

We submitted our IND for AAV-CNGB3 to the FDA in the fourth quarter of 2017. The IND was initially not opened because we received a question from the FDA regarding our injection device compatibility assay, thus putting the IND on clinical hold until we have satisfactorily answered the FDA's question and the clinical hold is lifted by the FDA. In the device compatibility assay the FDA noted a disparity between the target titer for the intended low dose dilution and the actual titer obtained on polymerase chain reaction, or PCR, analysis. The FDA requested clarification on whether this was an imprecise dilution scheme for the low dose or a PCR assay issue. We submitted a response to the FDA on May 2, 2018 providing data that identified the issue as a PCR assay artifact and also showing data that we believe supports that this has now been addressed. On May 31, 2018 the FDA released the clinical hold on our IND for AAV-CNGB3.

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

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

In adult *CNGB3* patients, treatment of the central retina with our AAV-CNGB3 product candidate via subretinal injection has been generally well tolerated. Following the review of the safety data for each cohort treated in this study, the independent monitoring committee, or IDMC, recommended escalation to the higher dose in the next cohort. Data from the first adult treatment cohort along with our preclinical data of AAV-CNGB3 was used to support our PRIME designation that was awarded by the EMA in February 2018.

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

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

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

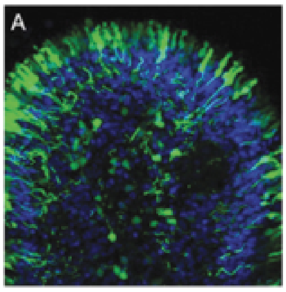
Our *CNGB3* gene therapy product candidate, AAV-CNGB3, was granted orphan drug designation by the FDA and EMA, as well as rare pediatric disease designation by the FDA for the treatment of achromatopsia caused by mutations in the *CNGB3* gene. We have also been granted PRIME designation by the EMA.

*ACHM Caused by Mutations in CNGA3*

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

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

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



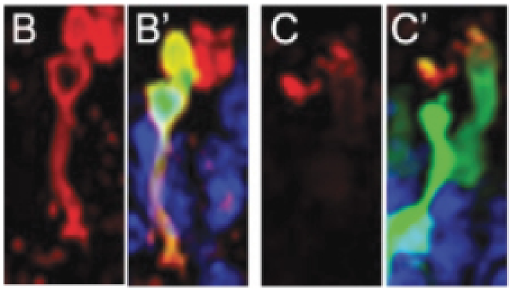




**Figure 4A.** An hPSC derived HMR showing GFP expression (green) driven by our promoter in human cones throughout the HMR.

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

**Figure 4B'.** An overlay of GFP expression from our 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 4C.** The red marker identifies M/red and L/green cones.

**Figure 4C'.** 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 mutant mice lacking the *Cnga3* gene conducted at UCL IO during 2017 and 2018, treatment of retinas of *Cnga3* mutant mice with AAV-CNGA3 was associated with restoration of the cone electrical response following subretinal delivery. Figure 5 and Figure 6 show the rescue of cone function that was observed in two of these studies with doses spanning those proposed in the clinical trial and in a dose dependent manner. We believe this supports the evaluation of AAV-CNGA3 to treat patients with ACHM caused by mutations in *CNGA3* in a Phase 1/2 clinical trial. The data from these studies have not been published.

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

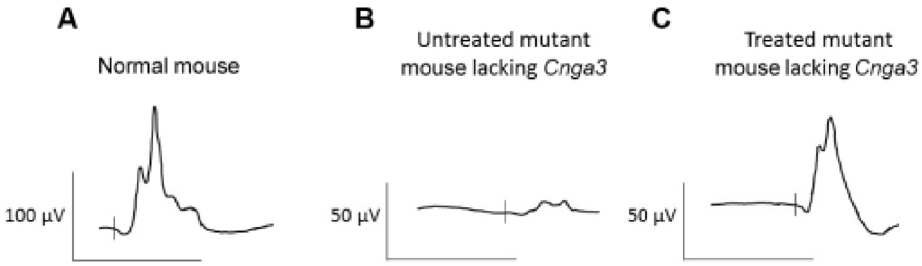



**Figure 5**. Cone electrical response in mice retinas reacting to a single flash of bright light, measured by ERG.

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

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

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

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

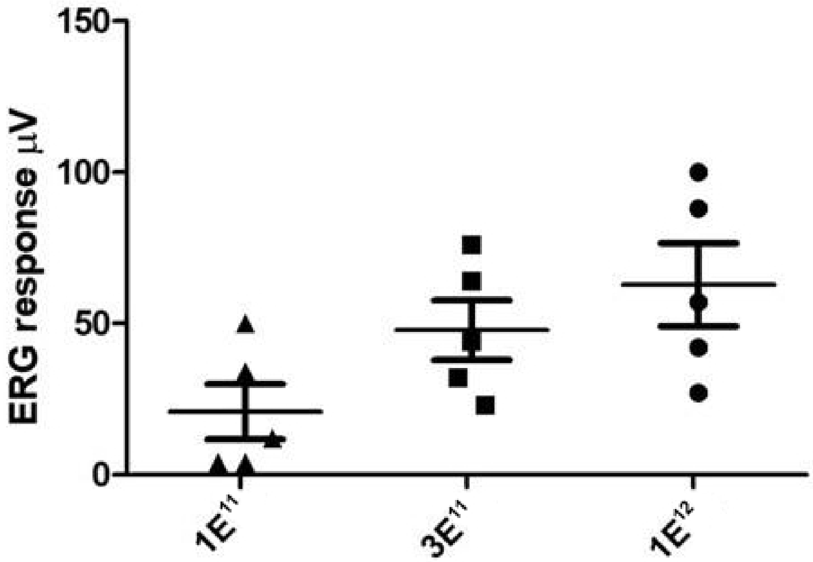



**Figure 6**. The photopic ERG amplitudes measured to assess cone photoreceptor function in *Cnga3* mutant mice treated with AAV-CNGA3 at doses of $1E^{11}$ vg/mL (n=5), $3E^{11}$ vg/mL (n=5) and $1E^{12}$ vg/mL (n=5). Mice were treated at 15 days post-natal and ERGs were assessed four weeks following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

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

*Clinical development of AAV-CNGA3*

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

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

***X-Linked Retinitis Pigmentosa***

*Disease Background and Market Opportunity*

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

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

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

*Our Gene Therapy Program*

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

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

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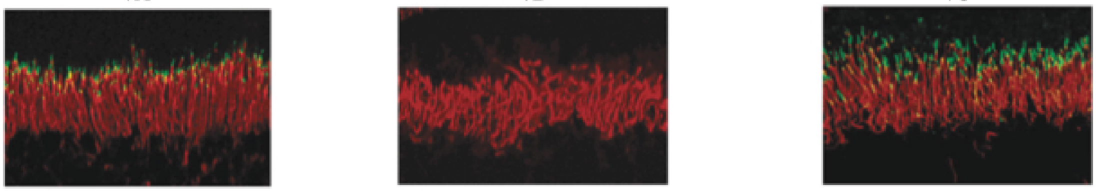
Figure 7 and Figure 8 show data from these preclinical studies regarding the effect of subretinal delivery of AAV-RPGR containing our stabilized *RPGR-ORF 15* in mice lacking the *Rpgr* gene. In these studies, different color stains were used to investigate the restoration of (i) RPGR protein expression,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

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

7A 7B 7C



Normal RPGR expression | Untreated mutant lacking RPGR | Treated mutant lacking RPGR

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

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

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

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

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

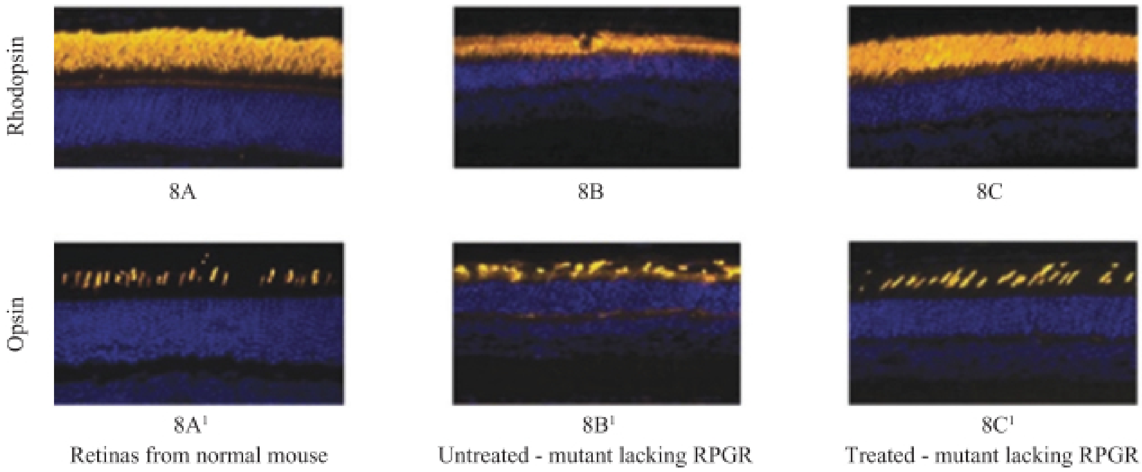



**Figure 8.** In these preclinical mouse experiments, a yellow tag reveals the location of the opsins.

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

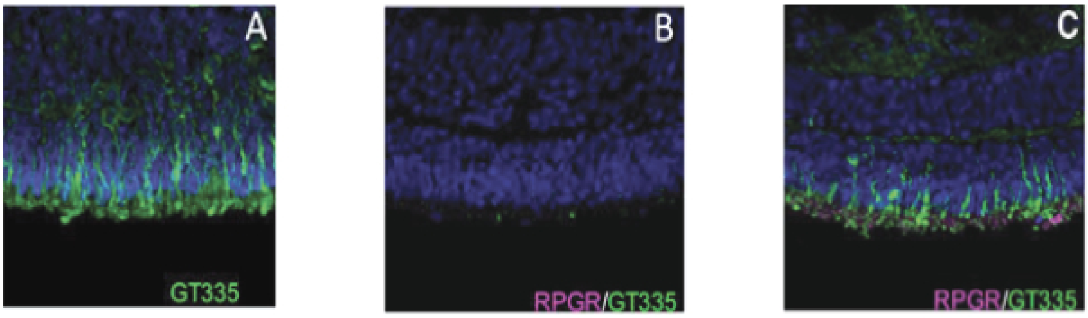
**Figures 8B and 8B'.** *Rpgr* mutant mouse retina showing the localization of rhodopsin and opsin.

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

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

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

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




Derived from normal patient | Untreated - Derived from XLRP-RPGR patient | Treated - Derived from XLRP-RPGR patient

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

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

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

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

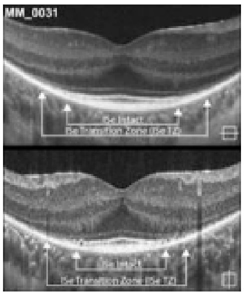
To support the advancement of AAV-RPGR into clinical development, we conducted three single-dose toxicology studies from January 2016 to August 2017 at UCL IO. We performed a six month toxicology study in normal mice delivering doses of saline in both eyes for the control (n=5), and doses of AAV-RPGR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

*Clinical Development of AAV-RPGR*

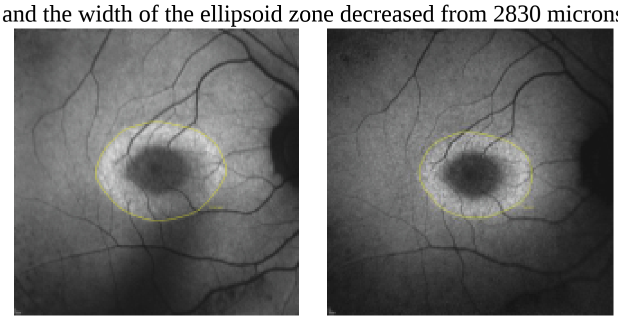
We have an ongoing natural history study in XLRP-RPGR including approximately 100 patients, which allows us to collect structural and functional data for up to five years on prospectively defined endpoints, including functional tests (visual acuity and contrast sensitivity), retinal imaging (color fundus photography, fundus autofluoresence imaging, spectral domain optical coherence tomography, adaptive optics and visual field testing) and electrophysiological assessments. The study centers are the Moorfields Eye Hospital in London, the Kellogg Eye Center at the University of Michigan, the Medical College of Wisconsin & Froedtert Hospital and Massachusetts Eye and Ear. We believe access to this large population of XLRP-RPGR patients has enabled us to efficiently enroll appropriate patients into our XLRP-RPGR Phase 1/2 clinical trial. In addition to giving us access to patients and potentially accelerated enrollment in our treatment studies, we believe the prospective natural history data on each treated patient will allow us to gather robust data from our Phase 1/2 clinical trial in a condensed timeframe. Of particular interest is the area and width of the ellipsoid zone, which is a validated surrogate marker of retinal degeneration in RP and other IRDs.

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

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




10A



10B

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

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

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

A further benefit of the XLRP-RPGR natural history study is access to longitudinal data from the population of XLRP-RPGR patients over time. Figure 11 is a graph of data collected in our XLRP-RPGR natural history study of individual patients, which evidence a relationship between a patient's ellipsoid zone width and age. These data show a reduction in ellipsoid zone width over time in each patient, as well as the increased rate of decline in younger individuals. We believe these data will support both our Phase 1/2 clinical trial and any future pivotal trial by enabling us to select patients with similar characteristics and rate of disease progression for treatment with AAV-RPGR, as well as providing longitudinal and individual patient data on the rate of ellipsoid zone shrinkage to more readily assess the impact of therapeutic intervention.

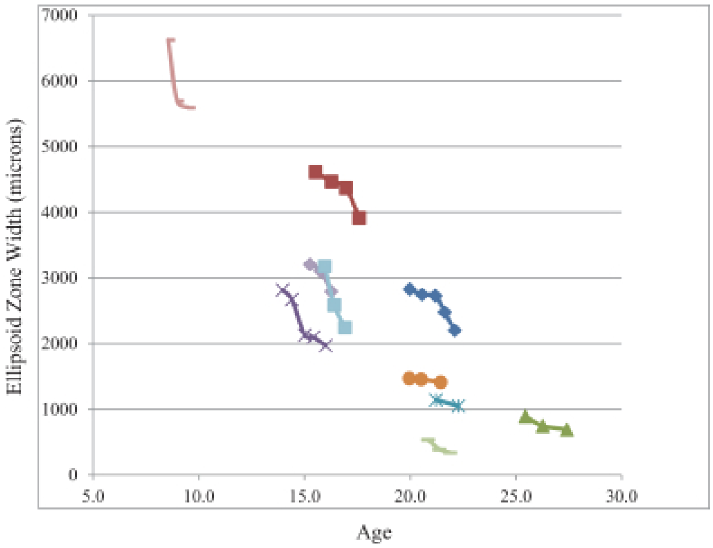



**Figure 11.** Graph of data gathered in our XLRP-RPGR natural history study showing the correlation between ellipsoid zone width (Y-axis) and age (X-axis) in individual patients.

We are conducting a Phase 1/2 clinical trial of AAV-RPGR in both adult and pediatric XLRP-RPGR patients. This trial is open in the United Kingdom under our CTA and United States under our IND. In the dose escalation phase of the trial, up to 18 adult patients may be administered one of three different doses of vector in dose escalating cohorts of three to six patients at a time. Once an acceptable safety profile has been established in adults, up to 18 adults or children may then be treated at an acceptable dose. We expect to begin enrolling patients in this expansion cohort in the second half of 2018. The primary endpoint of this open-label, dose-escalation clinical trial is the safety of delivering AAV-RPGR through subretinal injection. Secondary endpoints include the outcomes of a range of functional tests, quality of life measures and detailed analysis of the retina, including structural analysis of individual photoreceptors and measurements of ellipsoid zone via optical coherence tomography and fundus autofluorescence ring size. Following discussions with the FDA, we will be splitting the extension cohort into two groups to be treated with two different doses of AAV-RPGR. We will look at a range of functional and structural assessments including the ellipsoid zone progression as an acceptable surrogate marker of retinal degeneration with the aim of gaining early data on the activity of our potential gene therapy product in this patient population. Retinal images of treated and untreated fellow eyes at different time-points will be read at an independent reading center and evaluators will be blinded to treatment.

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

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

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

We anticipate completing adult dosing in this Phase 1/2 clinical trial during the third quarter of 2018, and completing the dosing of the two pediatric cohorts in 2019. We expect preliminary data from the dose escalation phase to be available during the first half of 2019.

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

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

***RPE65*-Deficiency**

*Disease Background and Market Opportunity*

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

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

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

*Our Gene Therapy Program*

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

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

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

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

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

We conducted four single-dose toxicology and biodistribution studies of AAV-RPE65 from January 2015 to December 2016. We performed a long-term toxicology study in normal mice in which four eyes were dosed with saline as a control and nine eyes were dosed with AAV-RPE65 at $4E^{9}$ vg/eye, with a toxicology assessment at one, three, six and nine months post-administration. We also conducted an eight week mouse study, an eight week rabbit study and an eight week minipig study. In the mouse study, 15 mice were dosed in both eyes with saline as a control, 15 mice were dosed in both eyes with AAV-RPE65 at $1.2E^{9}$ vg/eye and 15 mice were dosed in both eyes with AAV-RPE65 at $3.7E^{9}$ vg/eye, providing five mice from each group for studying local and systemic effects at each time-point of one, four and eight weeks after treatment. In the rabbit study, nine rabbit's right eyes were dosed for each group with a saline control group, a $0.6E^{11}$ vg/eye group and a $1.9E^{11}$ vg/eye group, providing three animals from each group for studying local and systemic effects at each time-point of one, four and eight weeks after treatment. The minipig study was a two week single dose injection study in minipigs (n=2, each dosed in one eye) at a dose of $1.84E^{10}11$ vg/eye. The minipig study was performed by Charles River Laboratories, while the other three studies were performed at UCL IO. No harmful effects on the retina were observed during these studies. We used these data in support of our CTA and IND for treatment of *RPE65*-deficient patients with AAV-RPE65.

*Clinical development of AAV-RPE65*

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

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

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

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

In each patient treated in cohort one, we observed improvement or stability in central visual function following treatment compared to baseline and compared to the untreated fellow eye. Retinal sensitivity was measured with threshold static perimetry using Octopus 900 perimetry and visual field modelling and analysis, or VFMA. Observations at 18 months following vector administration in the first cohort have demonstrated a potential increase in retinal sensitivity by up to 40% from baseline. In contrast, we observed that the untreated eyes of patients in this cohort suffered a reduction in retinal sensitivity of up to 40%, which is in consistent with data from our parallel prospective natural history study of *RPE65*-deficient patients. In addition to the perimetry and VFMA data, improvements in time and error rate in mobility maze navigation have been observed in these patients at six and 12 months following treatment. However, this is preliminary data and needs to be supported by data collected at later time-points and in larger numbers of patients.

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

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

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

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

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

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

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

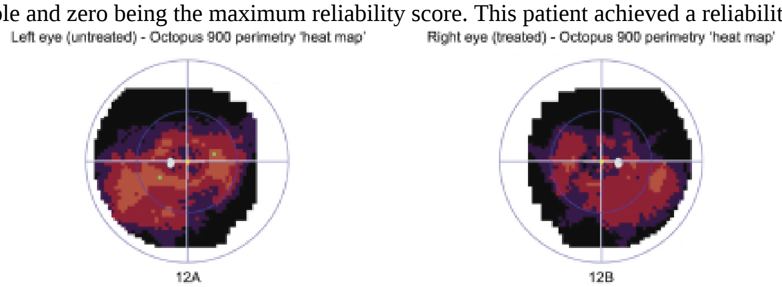



**Figure 12.** Image of the 'heat map' left and right eyes of an 11 year old patient produced prior to treatment with AAV-RPE65.

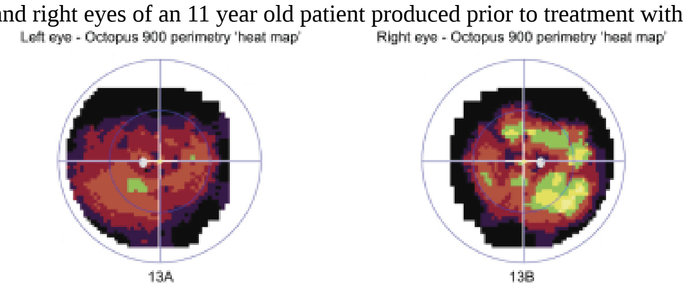



**Figure 13.** Image of the heat map left and right eyes of an 11 year old patient produced three months following treatment with AAV-RPE65 in the right eye, the left eye was untreated.

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

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

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

***LCA4***

*Disease Background*

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

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

*Our Gene Therapy Program*

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

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

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

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

It was observed at both time-points that *Aipl1* mutant mice treated with AAV-AIPL1 suffered less photoreceptor loss than untreated *Aipl1* mutant mice, with the retinas of untreated mutant mice almost completely degenerated by 24 months of age. *Aipl1* mutant mice were treated with .5uL of AAV-AIPL1 at 1E12 at four weeks post-natal and eyes were sectioned at six months and 23 months after treatment. These treated retinas were compared to retinas from untreated control *Aipl1* mice (n=17 eyes), and retinas from normal mice without the *Aipl1* mutation sectioned at the same post-natal ages as the treated *Aipl* mutant mice. The data indicates that subretinal administration of AAV-AIPL1 is associated with the protection of the retina from degradation that occurs in *Aipl1* mutant mice, and this effect was durable out to two years, the oldest age studied in these mice.

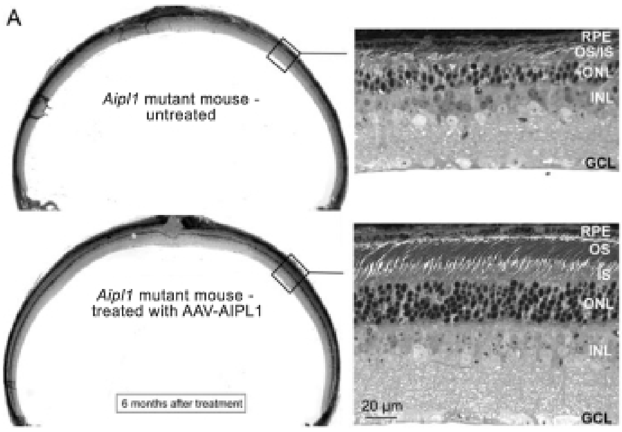



**Figure 14.** Histological sections of retinas of *Aipl1* mutant mice treated with AAV-AIPL1 six months after treatment with AAV-AIPL1, compared to untreated retina. The top image is the retina of an untreated *Aipl1* mutant mouse at seven months post-natal. The lower image is the retina of a *Aipl1*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

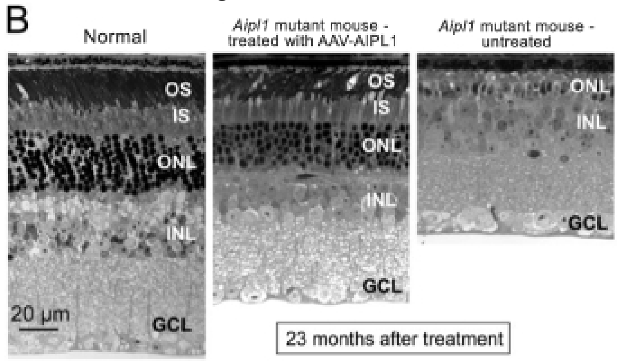



**Figure 15.** Histological sections of retinas of *Aipl1* mutant mice treated with AAV-AIPL1 23 months after treatment with AAV-AIPL1, compared to untreated retina and retina from a normal mouse. The left image is the retina of an normal mouse at 24 months post-natal. The middle image is the retina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

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

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

Our product candidate, AAV-AIPL1, was manufactured and released for compassionate use under a specials license in the UK to treat LCA4 patients at the Moorfields Eye Hospital. This allows physicians at the

Moorfields Eye Hospital to prescribe a treatment of AAV-AIPL1 for LCA4 patients they deem appropriate. We play no role in the physician's treatment decision. We intend to use the data produced by the compassionate use treatment to inform any potential clinical development plan as well as any interactions with the regulatory agencies that would enable us to make this intervention more widely available to the LCA4 patient population. Although patients have been reviewed at the Moorfields Eye Hospital, so far none have been treated with AAV-AIPL1. As the manufacturer of AAV-AIPL1 under a specials license, we have a record retention requirement and a continuing obligation to inform the MHRA of any suspected adverse reaction to our medicinal product which is a serious adverse reaction.

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

Manufacturing a special also imposes a five year record retention requirements subject to review by the MHRA, including details of any suspected adverse reaction to the product so sold or supplied of which the person is aware or subsequently becomes aware, as well as a continuing obligation to notify the MHRA of any suspected adverse reaction to the medicinal product which is a serious adverse reaction.

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 85% of patients who receive radiation treatment for head and neck cancer experience reduced saliva production during treatment, and approximately 40% of those patients who remain cancer free for two or more years after treatment continue to suffer from grade 2 or 3 RIX. There are approximately 170,000 such patients in the United States, with approximately 10,000 new cases each year. Severity of RIX is measured from grade 1 (mildest) to 4 (most severe). As these patients tend to be under the care of a physician and dentist and have access to some form of health insurance, we believe this is an accessible indication with much larger commercial potential than some genetic diseases that are currently targets of our gene therapy programs.

RIX is a frequent side effect of head and neck cancer treatment because the standard treatment of locally advanced head and neck cancer involves radiotherapy, which can cause irreversible damage to non-diseased tissues located near oral tumors, such as the salivary glands. The fluid secreting, or acinar cells, of the salivary glands are uniquely sensitive to radiation, are destroyed acutely on IR exposure and to a large extent do not regenerate, resulting in chronically reduced salivary output. Because saliva plays such a critical role in the physiology and protection of upper gastrointestinal, or GI, tract tissues, patients with chronic RIX suffer severe long term complications of head and neck irradiation that has a significant impact on the patient's daily living. Chronic RIX results in severe side effects, including difficulty swallowing, or dysphagia, oral discomfort, malnutrition, oral mucositis, changes in taste, increased oral infections and dental cavities.

*Our Gene Therapy Program—RIX*

Salivary glands are an attractive target organ for gene therapy treatments because they are self-contained, partially immune protected and easily accessible, allowing for non-invasive delivery of small vector doses.

We are developing AAV-AQP1 to treat RIX by increasing water conduction in the chronically damaged salivary glands by introducing a water conducting channel into the remaining epithelial cells of these damaged glands. Adequate water secretion by surviving epithelial cells has the potential to deliver the protective exocrine proteins produced by remaining gland cells into the mouth.

The key to our approach is that, unlike the water conducting acinar cells, the water impermeable duct cells of the glands appear to be resilient to IR exposure. As a consequence of this relative resilience to radiation treatment, salivary glands damaged by radiation treatment tend to contain mostly water impermeable ductal epithelial cells. To make these duct cells permeable to water, AAV-AQP1 introduces the gene for the human aquaporin water channel, or *hAQP1*. We have demonstrated that this has the potential to convey water permeability and causes ductal cells to generate an osmotic gradient, which causes them to secrete fluid into the lumen of the duct.

The proof of concept for this mechanism and its ability to increase the volume of saliva secreted by damaged salivary glands was observed in a Phase 1/2 clinical trial conducted by the U.S. National Institutes of Health, or NIH, in patients with chronic grade 2 or 3 RIX. The trial was designed as a short-term dose escalation trial of doses of AAV-AQP1 between $4.8E^7$ and $5.8E^9$ pu/gland using adenovirus as the vector to deliver the *hAQP1* to the remaining epithelial cells in the parotid gland of 11 patients suffering from chronic RIX. There were no reported severe adverse events among the patients treated, two out of three patients in each of the first three cohorts in this clinical trial were observed to have objective increases in saliva volume produced by the treated parotid gland, with increases in parotid flow ranging from 60% to 540%, and all but one of these patients showed a decrease in symptoms of dry mouth as measured by subjective visual analog scales, validated in other forms of xerostomia. The results of this study were published in *Proceedings of the National Academy of Sciences* in 2012.

We are currently conducting a Phase 1 dose escalation clinical trial in patients with grade 2 or 3 RIX who remain cancer free for at least five years after receiving radiation treatment. In this trial we are using AAV2 to deliver the *hAQP1* gene, as we believe AAV2 efficiently transfects the salivary gland cells and does not spread beyond the target cells. Up to 18 adult patients may be administered doses of AAV-AQP1 between $3E^9$ and $6E^{11}$ viral particles per gland in dose escalation cohorts of three patients each. The aim of the trial is to determine the safety of inserting *hAQP1* locally into the salivary glands of RIX patients, as well as to measure changes in salivary flow resulting from the introduction of this channel. We have completed dosing in the first cohort and begun dosing in the second cohort, having treated five patients. This clinical trial is being conducted in conjunction with the National Institute of Dental and Craniofacial Research at the NIH Dental Clinic.

We expect to initiate an additional clinical trial at Memorial Sloan Kettering Cancer Center in the second half of 2018.

The FDA granted orphan drug designation for AAV-AQP1 to treat symptoms of grade 2 and grade 3 late xerostomia from parotid gland hypofunction caused by radiotherapy for cancer of the oral cavity.

*Sjogren's Syndrome*

The destruction of salivary tissue resulting in chronic xerostomia may also be caused by chronic autoimmune disease. Sjogren's syndrome is an autoimmune disease in which a patient's immune system may target the salivary glands. Chronic inflammation of the salivary glands results in long term damage and chronic xerostomia in many Sjogren's patients. Data from preclinical studies in animal models of Sjogren's syndrome and data from explants of minor salivary glands of Sjogren's patients suggest that Sjogren's syndrome may also be treatable with our AAV-AQP1 vector. Supported by data from our preclinical studies and our ongoing RIX clinical trials, we anticipate initiating a clinical trial of AAV-AQP1 for xerostomia caused by Sjogren's syndrome in 2019.

**Neurodegenerative Diseases**

We also have research and preclinical programs targeting neurodegenerative diseases, with a research focus in ALS and Alzheimer's disease. In each of these diseases, we aim to target what we believe is a central factor in the underlying cell biology of the diseases, specifically RNA metabolism in ALS and endosomal trafficking dysfunction in Alzheimer's disease. Relying on our expertise in viral vector design, delivery, production and manufacturing, we are aiming to develop and optimize vectors to effectively treat both genetic and sporadic forms of these diseases.

***ALS***

*Disease Background and Market Opportunity*

ALS is a devastating, progressive, neurodegenerative disease leading to the loss of motor neurons, which are the neurons that control the ability to move, speak, swallow and ultimately to breathe. The gradual paralysis in ALS invariably leads to death. While 10% of ALS cases are caused by inherited genetic mutations, most ALS occurs sporadically, with no known genetic cause. Mutations in over 20 genes have been identified that cause the inherited ALS cases. Characterization of these disease-causing genes have implicated several cellular pathways in the disease, with a prominent role emerging for genes involved in the cellular control of RNA. Many new regulatory roles are being discovered for RNA, particularly in neurons.

One gene linked to ALS is the transactive response DNA-binding protein 43, or *TDP-43*. The TDP-43 protein is one of a number of proteins that binds to cellular RNA and regulates its function and stability. When *TDP-43* does not function normally, RNA regulation in the neurons loses its tight control and the motor neurons die. While mutations in *TDP-43* account for only about 0.5% of ALS cases, aggregates of TDP-43 protein are observed in motor neurons of more than 95% of all ALS patients, including both inherited and sporadic, and TDP-43 aggregation is a central feature of diseased motor neurons in ALS patients. *TDP-43*, therefore, may be a critical therapeutic target for the treatment of both sporadic and inherited forms of ALS. TDP-43 aggregates are also seen in approximately 50% of patients with frontotemporal dementia, or FTD, suggesting a potentially similar underlying mechanism of this neurodegenerative disease.

*Our Gene Therapy Approach*

Genetic approaches using yeast as the primary model system have been used to identify ways of protecting motor neurons from death in ALS. A genetic screen was conducted to look for activated genes that rescue the toxicity of TDP-43 aggregation. A group of 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 C9*orf*72. Improvements in ALS-like symptoms related to limb strength and mobility in rodent models of ALS have also been observed following administration of AAV-UPF1.

We believe that gene therapy using AAV-UPF1 may increase *UPF1* levels in cells affected by ALS, and we intend to deliver our viral vector product candidate to the central nervous system via intrathecal injection, or injection into the spinal canal. We are currently conducting IND enabling studies in animal models and have observed the preservation of neurons and a positive impact on functional endpoints in Fus and TDP-43 neuronal cell cultures. Data is expected to become available on studies regarding modes of central nervous system delivery in non-human primates during 2018 and head-to-head non-human primates capsid study is set to launch during the second half of 2018. In the second half of 2018 we anticipate initiating manufacturing for our ALS program and engaging the FDA in pre-IND discussions, with the goal of filing an IND and initiating a clinical trial of AAV-UPF1 in ALS patients in 2019.

***Alzheimer's Disease***

*Disease Background and Market Opportunity*

With the world population aging, Alzheimer's disease has emerged as an extremely common and costly disease. While some treatments that have temporary effects on Alzheimer's disease symptoms are available, there is currently no approved treatment that halts the progression of the disease. Two biological pathways have been identified that are considered causes of Alzheimer's disease. They are identified as causative because mutations in genes that affect these pathways alone cause patients to develop the disease. The first causative pathway, identified in rare forms of early onset Alzheimer's disease, is the misprocessing of amyloid precursor protein, or APP, caused by genetic defects in *APP* itself and the APP processing proteins presenilin 1 and 2. The second causative pathway is related to the correct movement, or trafficking, of cellular protein which is controlled by a cell component called the endosome. Loss of function mutations in the endosomal protein sortilin-related receptor 1, or *SORL1*, have recently been shown to cause Alzheimer's disease.

The endosome is an organelle within the cell that is responsible for correctly directing protein trafficking to different sites within the cell as well as to the cell surface. In neurons, there is significant protein trafficking, particularly at dendrites or neuronal connections where the endosomal trafficking system regulates the movement of the cell signaling machinery that allows neurons to communicate with one another.

The molecular machine that drives endosomal protein trafficking is made up of a complex of proteins together called the retromer. The protein encoded by the Alzheimer's disease causing gene *SORL1* is a retromer component. *SORL1* and other components of the retromer complex are commonly deficient in Alzheimer's disease patients' brains. Defects in the endosomal trafficking pathway have also been implicated in other neurodegenerative diseases, including Parkinson's disease, ALS and frontotemporal dementia.

*Our Gene Therapy Approach*

Our Alzheimer's disease program focuses on the endosomal trafficking pathway. In preclinical studies, we observed that increasing levels of key retromer proteins may reverse endosomal trafficking defects. We are identifying suitable retromer targets for gene augmentation in pre-symptomatic Alzheimer's patients.

There are several reasons why gene therapy is, in principle, well suited for Alzheimer's disease and other neurodegenerative diseases. The first relates to the pathophysiology, time course, and anatomical spread of these disorders. Neurodegenerative diseases generally begin locally in selectively vulnerable regions with "cell sickness" years before rampant cell death and wide-spread anatomical distribution. To be most effective, we believe interventions should be 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 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. In May 2018, we were granted a license to manufacture gene therapy product candidates in our cGMP compliant manufacturing facility by the UK Medicines and Healthcare products Regulatory Agency.

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 April 30, 2018, we own, have an exclusive license or co-exclusive license under, or an exclusive option to license 27 United States and foreign issued patents and 93 patent applications, pending in the United States and internationally. For any individual patent, the term depends on the applicable law in the country in which the patent is granted. In most countries where we have filed patent applications or in-licensed patents and patent applications, patents have a term of 20 years from the application filing date or earliest claimed non-provisional priority date. In the United States, the patent term is 20 years but may be shortened if a patent is terminally disclaimed over another patent that expires earlier. The term of a U.S. patent may also be lengthened by a patent term adjustment, in order to address administrative delays by the United States Patent and Trademark Office in granting a patent. In the United States, the term of a patent that covers an FDA-approved drug or biologic may be eligible for patent term extension in order to restore the period of a patent term lost during the premarket FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the natural expiration of the patent. The patent term restoration period is generally equal to the regulatory review period for the approved product which period occurs after the date the patent issued, subject to certain exceptions. Only one patent may be extended for a regulatory review period for any product, and the application for the extension must be submitted prior to the expiration of the patent. In the future, we may decide to apply for restoration of patent term for one of our currently owned or licensed patents to extend its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

*Company-Owned Intellectual Property*

We own six patent families relating to gene regulation platform technologies developed by us. The first patent family, includes 21 pending patent applications with claims directed to compositions of matter and methods of use in the United States, Europe, Australia, Canada, China, India, Japan, Brazil, Egypt, Indonesia, Israel, Republic of Korea, Malaysia, Mexico, New Zealand, Vietnam, African Regional IPO, Philippines, Singapore, South Africa and Eurasia. Patents issued from this family are expected to expire February 2, 2036, not including any patent term adjustments that may extend the patent term in certain jurisdictions. The other five families include five international applications relating to different gene regulations platform technologies with claims directed to compositions of matter and methods of use. We expect to convert each of these international applications to U.S. and international patent filings in due course. Patents issued from these five patent families are expected to expire in 2037 and 2038, not including any patent term adjustments that may extend the patent term in certain jurisdictions.

*Licensed Intellectual Property*

Certain of our issued patents and pending patent applications are exclusively licensed to us from UCLB and Brandeis.

*UCLB*

The UCLB portfolio includes three licensed patent families relating to our *RPE65*, *CNGA3*, and *RPGR* gene therapy programs and one optioned patent family relating to our dry AMD gene therapy program with a combined 46 pending patent applications.

The first patent family, with claims directed to compositions of matter and methods of use relating to our *RPE65* program, and the AAV-RPE65 product candidate includes 17 pending patent applications in the United States, Europe, Australia, Canada, China, India, Japan, Brazil, Egypt, Israel, Malaysia, Mexico, New Zealand, Nigeria, Philippines, Singapore, and Thailand. Patents issued from this family are expected to expire February 8, 2036, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

The second patent family, with claims directed to compositions of matter and methods of use relating to our achromatopsia program and the AAV-CNGA3 product candidate, includes one pending patent application, which we expect to convert to an international application and subsequent U.S. and international patent filings in due course. Patents issued from this family are expected to expire in 2039, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

The third patent family, with claims directed to compositions of matter and methods of use relating to our retinitis pigmentosa program and the AAV-RPGR product candidate, includes five pending applications in the United States, Europe, Canada, China, and Japan. Patents issued from this family are expected to expire in July 2035, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

The fourth patent family which we have optioned, with claims directed to compositions of matter and methods of use relating to our dry AMD gene therapy program, includes 23 pending applications in the United States, Europe, Australia, Canada, China, India, Japan, Brazil, Egypt, Indonesia, Israel, Republic of Korea, Malaysia, Mexico, New Zealand, Nigeria, Vietnam, African Regional IPO, Philippines, Singapore, South Africa, Thailand and Eurasia. Patents issued from this family are expected to expire February 2036, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

*Brandeis*

The licensed Brandeis portfolio includes one patent family with claims directed to compositions of matter and methods of use relating to our ALS gene therapy program and the AAV-UPF1 product candidate. This patent family includes an issued patent in Australia and pending patent applications in the United States, Europe, Canada and Hong Kong. Patents issued from this family are expected to expire October 8, 2033, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

**License Agreements**

***License Agreement between Athena and UCLB***

In February 2015, Athena entered into a license agreement with UCLB (the license agreement, together with all applicable amendments, is referred to as the First UCLB License Agreement, and together with all addendums, the First UCLB Agreement). In March 2016, all of Athena's rights, obligations, and liabilities under the First UCLB Agreement and all of its subsequent amendments, supplements, addendums and modifications were novated to us under a deed of novation. Pursuant to the First UCLB Agreement, UCLB granted Athena an exclusive, worldwide, and sublicensable license under certain intellectual property rights controlled by UCLB related to our *RPE65* and *CNGA3* and *CNGB3* gene therapy programs, including certain patent filings with claims directed to compositions of matter and methods of use relating to our *RPE65* program and the AAV-RPE65 product candidate, to develop and commercialize licensed products in the field of ocular gene therapy. We must use diligent efforts to develop and commercialize the licensed products.

In addition, under the terms of the First UCLB Agreement, we have an exclusive option to negotiate and enter into license addendums, or Athena Addendums, pursuant to which we would obtain royalty-bearing licenses under certain additional intellectual property rights, including certain patent filings relating to our dry AMD gene therapy program, on reasonable commercial terms. Such option expires on February 4, 2019.

Under the terms of the First UCLB Agreement, we issued a certain number of our ordinary shares to UCLB in accordance with a certain shareholder's agreement, or the Athena Shareholders' Agreement. We are also required to pay UCLB sales milestone payments of up to a total of £39.75 million in the aggregate and an annual management fee of £50,000 until certain royalty payments have been paid.

Commencing on the first commercial sale of licensed products, we must make low single-digit percentage royalty payments to UCLB on net sales of such products. Our royalty obligations under the agreement continue on a licensed product-by-licensed product and country-by-country basis until the earlier to occur of (a) the expiration of the last valid claim of a patent claiming such licensed product in such country, or (b) the 10th anniversary of the first commercial sale of such licensed product in such country. In addition, we must pay UCLB mid-twenty percentages of certain sublicensing revenues.

Unless terminated earlier, the First UCLB License Agreement will remain in effect until the expiration or termination of the last Athena Addendum. The First UCLB License Agreement may be terminated: (a) by either party in the event of the other party's material breach that remains uncured for 30 days (or for 14 days in the case of breaches related to payment obligations), (b) by 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.

Unless terminated earlier, each Athena Addendum will remain in effect on a country-by-country basis until the expiration of the last payment obligation under the First UCLB Agreement. Each Athena Addendum may be terminated: (a) by either party in the event of the other party's material breach that remains uncured for 30 days (or for 14 days in the case of breaches related to payment obligations), (b) by UCLB if we fail to achieve any of the milestone events in the applicable Athena Addendum within six months after the applicable milestone deadline, (c) immediately by UCLB if we challenge the validity or ownership of UCLB's patents, (d) by UCLB if we fail to provide an updated development plan for the relevant Athena Addendum within six months of the effective date of such Athena Addendum, (e) immediately by UCLB if we are in persistent breach of the relevant Athena Addendum and the parties fail to agree upon a mechanism to remedy such persistent breach (or we do not comply with such agreed upon mechanism), or (f) immediately by UCLB if we are in material breach of the relevant Athena Addendum more than twice in any 24-month period, even if such breaches have been remedied. Each Athena Addendum may also be terminated, or the exclusive licenses granted under the relevant Athena Addendum may be converted to a non-exclusive license, by UCLB upon three-months' notice if we, based on an independent expert determination, fail to use diligent efforts to achieve certain milestone events or to develop and commercially exploit licensed products and do not cure such failure within a certain cure period.

***License Agreements with UCLB***

*July 2017 Agreement with UCLB*

In July 2017, we entered into a license agreement with UCLB, or the Second UCLB Agreement. Pursuant to the Second UCLB Agreement, UCLB granted us an exclusive, worldwide, and sublicensable license under certain intellectual property rights, including certain patent filings, controlled by UCLB with claims directed to compositions of matter and methods of use relating to our retinitis pigmentosa gene therapy program and the AAV-RPGR product candidate to develop and commercialize licensed products in the field of ocular gene therapy. We must use diligent efforts to develop and commercialize the licensed products. Under the terms of the Second UCLB Agreement, we paid an initial upfront payment of $17,888. We are also required to pay UCLB sales milestone payments of up to a total of £39.75 million in the aggregate and an annual management fee of £50,000 until certain royalty payments have been paid.

Commencing on the first commercial sale of licensed products, we must make low single-digit percentage royalty payments to UCLB on net sales of such products. Our royalty obligations under the agreement continue on a licensed product-by-licensed product and country-by-country basis until the latest to occur of the expiration of the last valid claim of a patent claiming such licensed product in such country, the expiration of regulatory exclusivity for such licensed product in such country, or the 10th anniversary of first commercial sale of such licensed product in such country. The Second UCLB Agreement will remain in effect on a country-by-country basis until the expiration of the last payment obligation in such country. The Second UCLB Agreement may be terminated: (a) by either party in the event of the other party's material breach that remains uncured for 30 days, (b) by either party for the other party's insolvency, or (c) immediately by UCLB if we are in persistent breach of the Second UCLB Agreement and the parties fail to agree upon, within a reasonable amount of time, a mechanism to remedy such persistent breach (or we do not comply with such agreed upon mechanism), or (d) immediately by UCLB if we undergo certain change of control events or if we enter into a sublicense with certain prohibited persons which may adversely affect UCL's and/or UCLB's reputation. The Second UCLB Agreement may also be terminated or converted to a non-exclusive license by UCLB upon three months' notice if we, based on an independent expert determination, fail to use diligent efforts to develop and commercially exploit licensed products and do not cure such failure within a certain cure period.

*March 2018 Agreement with UCLB*

In March 2018, we, together with MeiraGTx UK II, entered into a license agreement with UCLB, or the Third UCLB Agreement. As of March 2018, the Third UCLB Agreement supersedes the Athena Agreement regarding the *CNGA3* program. Pursuant to the Third UCLB Agreement, UCLB granted us an exclusive, worldwide, and sublicensable license under certain intellectual property rights controlled by UCLB, including a certain patent filing with claims directed to compositions of matter and methods of use relating to our achromatopsia gene therapy program and the AAV-CNGA3 product candidate to develop and commercialize licensed products in the field of ocular gene therapy. We must use diligent efforts to develop and commercialize the licensed products.

Under the terms of the Third UCLB Agreement, we paid an initial upfront payment of £6,994, and issued certain number of shares with equivalent cash value of £100,000 to UCLB. We are also required to pay UCLB sales milestone payments of up to a total of £39.75 million in the aggregate and an annual management fee of £50,000 until certain royalty payments have been paid.

Commencing on the first commercial sale of licensed products, we must make low single-digit percentage royalty payments to UCLB on net sales of such products. Our royalty obligations under the agreement continue on a licensed product-by-licensed product and country- by-country basis until the latest to occur of the expiration of the last valid claim of a patent claiming such licensed product in such country, the expiration of any regulatory exclusivity for all licensed products in such country, or the tenth anniversary of first commercial sale of such licensed product in such country.

The Third UCLB Agreement will remain in effect on a country-by-country basis until the expiration of the last payment obligation in such country. The Third UCLB Agreement may be terminated: (a) by either party in the event of the other party's material breach that remains uncured for 30 days, (b) by either party for the other party's insolvency, (c) immediately by UCLB if we are in persistent breach of the Third UCLB Agreement and the parties fail to agree upon a mechanism to remedy such persistent breach (or we do not comply with such agreed upon mechanism), (d) immediately by UCLB if we fail to comply with certain obligations relating to the issuance of shares to UCLB under the Third UCLB Agreement, or (e) immediately by UCLB if we undergo certain change of control events or if we enter into a sublicense with certain prohibited persons, which may adversely affect 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. On December 31, 2015, we entered into an Agreement and Plan of Merger, or the BRI-Alzan Merger Agreement, with BRI-Alzan, and the Brandeis Agreement was assigned to us as a result of such merger. Pursuant to the terms of the BRI-Alzan Merger Agreement, we agreed to make cash payments to BRI-Alzan upon the achievement of certain milestones, subject to an aggregate cap of $4,500,000. In addition, we agreed to make low single-digit percentage royalty payments to BRI-Alzan on net sales of any product for the therapeutic or prophylactic treatment of ALS that is covered by a valid claim of the patent rights licensed under the Brandeis Agreement. The BRI-Alzan Merger Agreement includes customary confidentiality, indemnification, non-competition and non-solicitation provisions.

Pursuant to the Brandeis Agreement, Brandeis granted us an exclusive, worldwide license under certain patent rights with claims directed to compositions of matter and methods of use relating to our ALS gene therapy program and the AAV-UPF1 product candidate to develop and commercialize licensed products.

We must use commercially reasonable efforts to develop and commercialize licensed products. We also acquired non-exclusive, worldwide licenses to certain know-how controlled by Brandeis' to exploit licensed products. We are required to pay Brandeis developmental and regulatory milestone payments of up to a total of $1.0 million in the aggregate. We are also required to pay Brandeis annual license maintenance fees ranging from $15,000 to $100,000 depending on the development stage of the licensed product. Commencing on the first commercial sale of licensed products, we must make low single-digit percentage royalty payments to Brandeis on net sales of such products. In addition, we must pay Brandeis mid-teen percentages of sublicensing revenues.

The Brandeis Agreement will remain in effect on a country-by-country basis until the earlier of: (a) 1 year after the date that we, our affiliates or sublicensees last sell any licensed product in such country or (b) until the expiration of the last–to-expire of the licensed patent rights in such country. The Brandeis Agreement may be terminated by Brandeis for our insolvency or for our material breach that remains uncured for 60 days (or for 30 days in the case of breaches related to payment obligations). Such material breach may be cured only once in any 12-month period. Brandeis may also terminate any license granted under the Brandeis Agreement if we fail to timely achieve certain regulatory milestone events.

### *Trade Secrets*

We also rely on trade secrets, technical know-how and continuing innovation to develop and maintain our competitive advantage. Our policy requires inventors who are identified on any company-owned patent applications to assign rights to us. We also rely on confidentiality agreements with our employees, consultants and other advisors to protect our proprietary information. Our policy is to require third parties that receive material confidential information to enter into confidentiality agreements with us.

### *Trademarks*

Our trademark MeiraGTx has been registered in the European Union and a U.S. application is pending.

## Government Regulation and Product Approval

Governmental authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing, post-approval monitoring and reporting and export and import of products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, are extensive and require the expenditure of substantial time and financial resources.

### *FDA Approval Process*

We expect our future product candidates to be regulated as biologics. Biological products, including gene therapy products, are subject to extensive regulation by the FDA under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and other federal, state, local and foreign statutes and regulations. Both the FDCA and the PHSA and their corresponding regulations govern, among other things, the research, development, safety, testing, packaging, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of biological products. Before clinical testing of biological products in the United States may begin, we must submit an investigational new drug application, or IND, to the FDA, which reviews the clinical protocol, and the IND must become effective before clinical trials may begin. In some instances, we must also submit our protocols to the National Institutes of Health, or NIH, through its Recombinant DNA Advisory Committee, or RAC, for review before initiating clinical testing of gene therapy products.

Gene therapy products must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agencies before they may be legally marketed in foreign countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. The CBER works closely with the NIH and its RAC, which makes recommendations to the NIH on gene therapy issues and engages in a public discussion of scientific, safety, ethical and societal issues related to proposed and ongoing gene therapy protocols. The FDA has published guidance documents with respect to the development and submission of gene therapy protocols. The FDA also has published guidance documents related to, among other things, gene therapy products in general, their preclinical assessment, observing subjects involved in gene therapy clinical trials for delayed adverse events, potency testing, and chemistry, manufacturing and control information in gene therapy INDs.

To date, the FDA has approved three human gene therapy products for sale, including Kite Pharma's Yescarta, Novartis' Kymriah and Spark's Luxturna, and has provided general guidance regarding the development of gene therapy products. For example, the FDA has established the Office of Tissue and Advanced Therapies within CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee, to advise CBER on its reviews. In addition, the FDA has issued a growing body of clinical guidelines, chemical, manufacturing and control, or CMC, guidelines and other guidelines, all of which are intended to facilitate industry's development of gene therapy products.

Ethical, social and legal concerns about gene-editing technology, gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating biotechnology. More restrictive regulations or claims that our products are unsafe or pose a hazard could prevent us from commercializing any product candidates. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

*U.S. Biological Products Development Process*

The FDA determined that more than minimally manipulated products must be approved by the FDA through the Biologics License Application, or BLA, process before they may be legally marketed in the United States. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- completion of extensive nonclinical, sometimes referred to as preclinical laboratory tests, and preclinical studies and applicable requirements for the humane use of laboratory animals and formulation studies in accordance with applicable regulations, including good laboratory practices, or GLPs;

- submission to the FDA of an IND application, which must become effective before clinical trials may begin;

- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before the trial is commenced;

- performance of adequate and well controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;

- submission to the FDA of a BLA for marketing approval that includes substantive evidence of safety, purity, potency and efficacy from results of nonclinical testing and clinical trials;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with cGMP to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;

- potential FDA audit of the nonclinical and clinical study sites that generated the data in support of the BLA; and

- FDA review and approval, or licensure, of the BLA.

Before testing any biological product candidate, including a gene therapy product, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLPs. The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing and controls, information about product chemistry, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing, such as reproductive toxicity tests and carcinogenicity in animals, may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, after which human clinical trials may begin unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. With gene therapy protocols, if the FDA allows the IND to proceed, but a RAC decides that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trials. In addition to the IND submission process, sponsors of certain clinical trials of cells containing recombinant or synthetic nucleic acid molecules, including human gene transfer studies, must comply with the NIH's Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. The NIH Guidelines set forth the principles and requirements for NIH and institutional oversight of research with recombinant or synthetic nucleic acid molecules, including the standards for investigators and institutions to follow to ensure the safe handling and containment of such molecules. In April 2016, modifications to the NIH Guidelines went into effect, pursuant to which only a subset of human gene transfer protocols are subject to review by the RAC. Specifically, under the modified NIH Guidelines, RAC review of the protocol will be required only in exceptional cases where an oversight body such as an Institutional Biosafety Committee, or IBC, which provides local review and oversight of research utilizing recombinant or synthetic nucleic acid molecules, or an IRB determines that the protocol would significantly benefit from RAC review, and the protocol (a) uses a new vector, genetic material, or delivery methodology that represents a first-in-human experience and thus presents an unknown risk, and/or (b) relies on preclinical safety data that were obtained using a new preclinical model system of unknown and unconfirmed value, and/or (c) involves a proposed vector, gene construct, or method of delivery associated with possible toxicities that are not widely known and that may render it difficult for oversight bodies to evaluate the protocol rigorously. The RAC review proceedings are public, and reports are posted publicly to the website for the NIH's Office of Biotechnology Activities. Although compliance with the NIH Guidelines is mandatory for research conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Independent of RAC review, the NIH Guidelines also require all human gene transfer protocols subject to the NIH Guidelines to be registered with NIH, with limited exemptions. A study subject to the NIH Guidelines may not begin until the IBC approves the protocol, and the IBC cannot approve the protocol until confirmation from the NIH that such registration is complete. In the event that RAC review is warranted, the protocol registration process cannot be completed until RAC review has taken place.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, the efficacy measurements to be evaluated and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Clinical trials also must be reviewed by an IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biological product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- Phase 2. The biological product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.

- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

In most cases, the FDA requires two adequate and well controlled Phase 3 clinical trials to demonstrate the safety and efficacy of a biological product. In rare instances, a single Phase 3 trial, together with other confirmatory evidence may be sufficient to support a BLA submission. Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by ten years of annual queries, either in person or by questionnaire.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other trials, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend or permanently discontinue a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk or the clinical trial is not being conducted in accordance with FDA regulations. Similarly, an IRB can suspend or terminate approval of a clinical study at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product candidate has been associated with unexpected serious harm to patients. The FDA and the IRB may also halt, terminate or impose other conditions if either believes the patients are subject to unacceptable risk.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. 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 of 2017 was enacted, which, among other things, removes penalties for not complying with ACA's individual mandate to carry health insurance. There is still uncertainty with respect to the impact President Trump's administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, on May 11, 2018, President Trump laid out his administration's "Blueprint" to reduce the cost of prescription drugs while preserving innovation and cures. The Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. Although some of these, and other, proposals will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

*U.S. Foreign Corrupt Practices Act*

The U.S. Foreign Corrupt Practices Act of 1977, or FCPA, prohibits U.S. corporations and individuals from engaging in certain activities to obtain or retain business or secure any improper advantage, or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any employee or official of a foreign government or public international organization, or political party, political party official, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. The scope of the FCPA also includes employees and officials of state-owned or controlled enterprises, which may include healthcare professionals in many countries. Equivalent laws have been adopted in other foreign countries that impose similar obligations.

***Government Regulation Outside of the United States***

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application, or CTA, much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

*Clinical Trials*

Clinical trials of medicinal products in the European Union must be conducted in accordance with European Union and national regulations and the International Conference on Harmonization, or ICH, guidelines on GCPs. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products. If the sponsor of the clinical trial is not established within the European Union, it must appoint an entity within the European Union to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

Prior to commencing a clinical trial, the sponsor must obtain a clinical trial authorization from the competent authority, and a positive opinion from an independent ethics committee. The application for a clinical trial authorization must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. Currently, clinical trial authorization applications must be submitted to the competent authority in each EU Member State in which the trial will be conducted. Under the new Regulation on Clinical Trials, which is currently expected to take effect in 2019, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only a limited involvement. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be notified to or approved by the relevant competent authorities and ethics committees. Medicines used in clinical trials must be manufactured in accordance with cGMP. Other national and European Union-wide regulatory requirements also apply.

During the development of a medicinal product, the EMA and national medicines regulators within the European Union provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Scientific Advice Working Party of the Committee for Medicinal Products for Human Use, or CHMP. A fee is incurred with each scientific advice procedure. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical trials, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application of the product concerned.

*Marketing Authorizations*

To obtain regulatory approval of an investigational biological product under EU regulatory systems, we must submit a marketing authorization application. The application used to file the BLA in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements. The process for doing this depends, among other things, on the nature of the medicinal product.

The centralized procedure results in a single marketing authorization, or MA, granted by the European Commission that is valid across the EEA (i.e., the European Union as well as Iceland, Liechtenstein and Norway). The centralized procedure is compulsory for human drugs that are: (i) derived from biotechnology processes, such as genetic engineering, (ii) contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions and viral diseases, (iii) officially designated orphan medicines and (iv) advanced-therapy medicines, such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure may at the request of the applicant also be used in certain other cases. Therefore, the centralized procedure would be mandatory for the products we are developing.

The Committee for Advanced Therapies, or CAT, is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CAT is primarily responsible for the scientific evaluation of ATMPs and prepares a draft opinion on the quality, safety and efficacy of each ATMP for which a marketing authorization application is submitted. The CAT's opinion is then taken into account by the CHMP when giving its final recommendation regarding the authorization of a product in view of the balance of benefits and risks identified. Although the CAT's draft opinion is submitted to the CHMP for final approval, the CHMP may depart from the draft opinion, if it provides detailed scientific justification. The CHMP and CAT are also responsible for providing guidelines on ATMPs and have published numerous guidelines, including specific guidelines on gene therapies and cell therapies. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs; the manufacturing and control information that should be submitted in a marketing authorization application; and post-approval measures required to monitor patients and evaluate the long term efficacy and potential adverse reactions of ATMPs. Although these guidelines are not legally binding, we believe that our compliance with them is likely necessary to gain and maintain approval for any of our product candidates.

Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days. This excludes so-called clock stops, during which additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. At the end of the review period, the CHMP provides an opinion to the European Commission. If this is opinion favorable, the Commission may then adopt a decision to grant an MA. In exceptional cases, the CHMP might perform an accelerated review of an MAA in no more than 150 days (not including clock stops). This is usually when the product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation.

The European Commission may grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The European Commission may also grant a so-called "marketing authorization under exceptional circumstances". Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;

- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radio-pharmaceutical, by an authorized person; and

The package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal. A marketing authorization under exceptional circumstances should not be granted when a conditional marketing authorization is more appropriate.

The European Union medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain EU Member States may prohibit or restrict us from commercializing our products, even if they have been granted an MA.

*Data and Marketing Exclusivity*

The European Union also provides opportunities for market exclusivity. Marketing authorization applications for generic medicinal products do not need to include the results of preclinical and clinical trials, but instead can refer to the data included in the marketing authorization of a reference product for which regulatory data exclusivity has expired. In the European Union, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. The two-year period may be extended to three years if during the first eight years a new therapeutic indication with significant clinical benefit over existing therapies is approved. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the EU regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

There is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the European Union. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

*Orphan Medicinal Products*

Products receiving orphan designation in the European Union can receive ten years of market exclusivity. During the ten year market exclusivity period, the EMA cannot accept another application for a marketing authorization, or grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indication, in respect of a similar medicinal product. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers. The application for orphan drug designation must be submitted before the MAA. The applicant will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, an MA may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;

- the applicant consents to a second orphan medicinal product application; or

- the applicant cannot supply enough orphan medicinal product.

*Pediatric Investigation Plan*

In the EMA, MAAs for new medicinal products not authorized have to include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which an MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU Member States and trial results are included in the product information, even when negative, the product is eligible for a six-months supplementary protection certificate extension.

*Post-Approval Controls*

The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the marketing authorization. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions.

All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

*Pricing and Reimbursement*

Governments influence the price of medicinal products in the European Union through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other EU Member States allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription medicines, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

*PRIME Scheme*

In July 2016 the EMA launched PRIME scheme. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is however not guaranteed. The benefits of a PRIME designation includes the appointment of a rapporteur from the CHMP before submission of an MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

*UK Specials Regulation*

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

Manufacturing a special also imposes a five year record retention requirements subject to review by the MHRA, including details of any suspected adverse reaction to the product so sold or supplied of which the person is aware or subsequently becomes aware, as well as a continuing obligation to notify the MHRA of any suspected adverse reaction to the medicinal product which is a serious adverse reaction.

## Employees

As of March 31, 2018, we had 59 employees, including 11 employees with M.D. or Ph.D. degrees. Of these full-time employees, 45 are engaged in research and development activities. None of our employees is subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relationship with our employees to be good.

## Facilities

Our principal office is located at 430 East 29th Street, 10th Floor, New York, NY 10016, USA, where we lease 5,887 square feet of office space. We lease this office space under a lease that terminates on December 31, 2021.

We also lease the ground rights where our 29,000 square foot manufacturing facility is located, at 92 Britannia Walk, London N1 7NQ, United Kingdom. This lease terminates February 2, 2021 and we have the option to extend until February 2, 2026.

## Legal Proceedings

We are not subject to any material legal proceedings.

# MANAGEMENT

## Executive Officers and Directors

The following table sets forth certain information of each executive officer and non-employee director of MeiraGTx Limited, including their ages as of May 29, 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. | 55 | Chief Development Officer and Director |
| ***Non-employee Directors*** | | |
| Keith R. Harris, Ph.D. (1)(2)(3) | 65 | Chairman of the Board |
| Ellen Hukkelhoven, Ph.D. | 32 | Director |
| Arnold J. Levine, Ph.D. (2) | 78 | Director |
| Joel S. Marcus (1)(3) | 70 | Director |
| Neil Mendoza (1)(2)(3) | 58 | Director |
| Gregory S. Moss | 34 | Director |
| Thomas E. Shenk, Ph.D. | 71 | Director |

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

## Executive Officers

*Alexandria Forbes, Ph.D.* has served as our President, Chief Executive Officer and member of our board of directors since March 2015. Prior to joining MeiraGTx, Dr. Forbes served as Senior Vice President of Commercial Operations at Kadmon Holdings, Inc., a biopharmaceutical company, from September 2013 to April 2015, and currently serves as a member of its board of directors. Effective upon the effectiveness of the registration statement of which this prospectus forms a part, Dr. Forbes will resign from the board of directors of Kadmon Holdings, Inc. A subsidiary of Kadmon Holdings, Inc. is a holder of more than 5% of our outstanding shares. Prior to Kadmon Holdings, Inc., Dr. Forbes spent eleven years as a healthcare investor at Sivik Global Healthcare (formerly Argus Partners), a healthcare hedge fund, from August 2001 to November 2008, and at Meadowvale Asset Management, a healthcare hedge fund, from January 2010 to June 2012. Before entering the hedge fund industry, Dr. Forbes was a Human Frontiers/Howard Hughes postdoctoral fellow at the Skirball Institute of Biomolecular Medicine at NYU Langone Medical Center from March 1997 to September 2000. Prior to this, Dr. Forbes was a research fellow at Duke University, and also at the Carnegie Institute at Johns Hopkins University. Dr. Forbes received an M.A. in Natural Sciences from Cambridge University and a Ph.D. in Molecular Genetics from Oxford University. Our board of directors believes Dr. Forbes' extensive academic and clinical experience, as well as her knowledge of the industry, qualifies her to serve on our board of directors.

*Richard Giroux* has served as our Chief Operating Officer since March 2015. Mr. Giroux joined MeiraGTx from Sarissa Capital Management LP, an activist healthcare hedge fund, where he was a partner from March 2014 to March 2015. Prior to Sarissa Capital Management LP, Mr. Giroux was a founding partner and healthcare portfolio manager of Meadowvale Partners, a multi-strategy hedge fund, from January 2010 until June 2012. Prior to Meadowvale Partners, he was a partner at Sivik Global Healthcare (formerly Argus Partners), a healthcare hedge fund, from August 2001 to November 2008. Prior to that, he worked at investment banks Salomon Smith Barney and Goldman Sachs. Mr. Giroux received a B.A. in Economics from Yale University.

*Stuart Naylor, Ph.D.* has served as our Chief Development Officer and a member of our board of directors since April 2015. From April 2015 to April 2016, Dr. Naylor was Chief Executive Officer of Athena

Vision Limited, a biotechnology company. From June 2013 to April 2015, Dr. Naylor served as managing director of Coltivare Ltd., a healthcare consulting company. From 2008 to 2013, Dr. Naylor was Executive Director and Chief Scientific Officer of Oxford BioMedica plc, a gene therapy company. Prior to joining Oxford BioMedica plc, Dr. Naylor focused on translational cancer research at the Institute of Cancer Research in London. Dr. Naylor has a B.S.C. in microbiology and virology from the University of Warwick, an M.S. in Immunology from Kings College London, and a Ph.D. from the Imperial Cancer Research Fund laboratory studying ovarian cancer and cytokine biology. Our board of directors believes Dr. Naylor's extensive academic and clinical experience, as well as his knowledge of the industry, qualifies him to serve on our board of directors.

**Non-employee Directors**

*Keith Harris, Ph.D.* has served as a member of our board of directors since June 2015 and served as chairman of our board of directors since February 2018. Dr. Harris is a London-based investment banker and financier with a 25-year career as a senior corporate finance and takeover advisor. Since 1999, Dr. Harris has been the chairman of Keith Harris & Associates, a sports consulting firm. Dr. Harris previously served as Chief Executive Officer of HSBC Investment Bank from 1994 to 1999 and Seymour Pierce Holdings Limited, a subsidiary of which, Seymour Pierce Limited, was acquired in a pre-paid administration under U.K. law in 2013. Dr. Harris received a B.A. in business and economics from the University of Bradford and a Ph.D. in Economics from the University of Surrey. Our board of directors believes that Dr. Harris' financial knowledge and experience qualifies him to serve as a member of our board of directors.

*Ellen Hukkelhoven, Ph.D.* has served as a member of our board of directors since October 2017. Dr. Hukkelhoven currently serves as a Senior Analyst at Perceptive Advisors, a leading healthcare investment firm. Prior to joining Perceptive Advisors in 2013, Dr. Hukkelhoven received an A.B. in molecular biology from Princeton University and a Ph.D. in cancer biology from Memorial Sloan Kettering Cancer Center. Our board of directors believes that Dr. Hukkelhoven's academic and biotechnology investing experience qualifies her to serve as a member of our board of directors.

*Arnold J. Levine, Ph.D.* has served as a member of our board of directors since February 2016. Dr. Levine currently serves as a professor emeritus at the Institute for Advanced Study at Princeton University. Dr. Levine was a director of Imclone Systems Incorporated from 2000 to 2003. He was a professor in the Department of Molecular Biology at Princeton University from 1984 until 1996, where he was named the Harry C. Wiess Professor in Life Sciences and was the chairman of the department. Dr. Levine received a B.A. from Harpur College, State University of New York at Binghamton and a Ph.D. in microbiology from the University of Pennsylvania. Our board of directors believes Dr. Levine's expertise and experience serving as a director in the pharmaceutical sector and his academic background provides him with the qualifications and skills to serve on our board of directors.

*Joel S. Marcus* has served as a member of our board of directors since June 2015. Mr. Marcus founded Alexandria Real Estate Equities, Inc., a real estate investment trust, and currently serves as Executive Chairman after previously serving as its Chairman since May 2007, Chief Executive Officer since March 1997 and a director since its founding in 1994. Mr. Marcus also co-founded and leads Alexandria Venture Investments, LLC which is a strategic venture arm of Alexandria Real Estate Equities, Inc. and the managing member of a holder of more than 5% of our outstanding shares. Prior to founding Alexandria Real Estate Equities, Inc., Mr. Marcus specialized in corporate finance and capital markets, venture capital and mergers and acquisitions with special expertise in the biopharmaceutical industry. Mr. Marcus received a B.A. and a J.D. from the University of California, Los Angeles. Our board of directors believes that Mr. Marcus' extensive experience in the life science real estate industry and as a chief executive officer, as well as his training as a C.P.A. and attorney, provide him with the qualifications and skills to serve on our board of directors.

*Neil Mendoza* has served as a member of our board of directors since June 2015. In 1986, Mr. Mendoza founded the custom marketing and publishing agency Forward, subsequently renamed Bookmark Content and

Communications, a subsidiary of WPP plc. Mr. Mendoza is the Chairman of Victoria Private Investment Office, a London-based investment advisory firm, which he joined in 2010. He received a M.A. in Geography from Oxford University. Our board of directors believes Mr. Mendoza's extensive experience with investments provides him with the qualifications and skills to serve on our board of directors.

*Gregory S. Moss* has served as a member of our board of directors since May 2018. Mr. Moss joined Kadmon Holdings, Inc. in 2012 and has served as its Senior Vice President and Deputy General Counsel since 2012. He was also Acting General Counsel and Compliance Officer of MeiraGTx Limited from April 2015 to December 2016. He received a combined Bachelor of Arts and Bachelor of Laws degree from Macquarie University in 2007. Our board of directors believes Mr. Moss' experience serving as general counsel of a biopharmaceutical company provides him with qualifications and skills to serve on our board of directors.

*Thomas E. Shenk, Ph.D.* has served as a member of our board of directors since June 2015. Dr. Shenk has been the James A. Elkins Jr. Professor of Life Sciences in the Department of Molecular Biology at Princeton University since 1984. He received a B.S. from University of Detroit and a Ph.D. from Rutgers University. Dr. Shenk served on the board of directors of Merck and Co. Inc., a pharmaceutical company from 2001 to 2012. Dr. Shenk currently serves as a director of Vical Incorporated, a biopharmaceutical company, and Kadmon Holdings, Inc., a biopharmaceutical company. Effective upon the effectiveness of this registration statement, Dr. Shenk will resign from the board of directors of Kadmon Holdings, Inc. Our board of directors believes Dr. Shenk's expertise and experience serving as a director in the pharmaceutical sector and his academic background provides him with the qualifications and skills to serve on our board of directors.

**Family Relationships**

There are no family relationships among any of our directors or executive officers.

**Board Composition and Election of Directors**

***Director Independence***

Our board of directors currently consists of nine members. Our board of directors has determined that, of our nine directors, Keith Harris, Ellen Hukkelhoven, Arnold Levine, Joel Marcus, Neil Mendoza and Gregory Moss do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of The Nasdaq Stock Market LLC, or Nasdaq. The listing requirements of Nasdaq, "independent directors" must comprise a majority of our board of directors within one year of closing of this offering.

***Classified Board of Directors***

In accordance with our new articles of association that will go into effect upon the closing of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of shareholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. The election of directors will be by plurality of votes cast by the shareholders entitled to vote. Effective upon the closing of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be Arnold Levine, Gregory Moss and Thomas Shenk, and their terms will expire at our first annual meeting of shareholders following this offering;

- the Class II directors will be Ellen Hukkelhoven, Joel Marcus and Stuart Naylor, and their terms will expire at our second annual meeting of shareholders following this offering; and

- the Class III directors will be Alexandria Forbes, Keith Harris and Neil Mendoza, and their terms will expire at the third annual meeting of shareholders following this offering.

Our new articles of association that will go into effect upon the closing of this offering will provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control of our company.

***Board Leadership Structure***

Our board of directors is currently chaired by Keith Harris. 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. The lead director's responsibilities would include, but would not be 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 Select 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 Keith Harris, Joel Marcus and Neil Mendoza. Keith Harris 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 Keith Harris, Joel Marcus and Neil Mendoza meet the independence requirements of Rule 10A-3 under the Exchange Act and the applicable Nasdaq rules. Our board of directors has determined that each of Keith Harris and Joel Marcus 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 Keith Harris, Arnold Levine and Neil Mendoza. Keith Harris serves as the chairperson of the committee. Our board of directors has determined that each of Keith Harris, Arnold Levine and Neil Mendoza 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 Keith Harris, Joel Marcus and Neil Mendoza. Joel Marcus serves as the chairperson of the committee. Our board of directors has determined that Keith Harris, Joel Marcus and Neil Mendoza 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 Select 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.<br>President and Chief Executive Officer | 2017 | 450,000 | 490,000 | 165,969 | 16,200 | 1,122,169 |
| Richard Giroux<br>Chief Operating Officer | 2017 | 400,000 | 440,000 | 153,202 | — | 993,202 |
| Stuart Naylor, Ph.D. (4)<br>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 or by our chief executive officer with respect to Mr. Giroux. For 2017, the compensation committee, with respect to Dr. Forbes, and the chief executive officer, with respect to Mr. Giroux, determined not to make any such grants.

The following table sets forth the options granted to our named executive officers in the 2017 fiscal year.

| Named Executive Officer | 2017 Options Granted |
|---|---:|
| Alexandria Forbes, Ph.D. | 83,741 |
| Richard Giroux | 77,299 |
| Stuart Naylor, Ph.D | 12,883 |

In January 2018, the named executive officers were granted options to purchase our ordinary shares in the following amounts: Dr. Forbes 103,066, Mr. Giroux 96,624 and Dr. Naylor 90,182. 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 275,081 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 Executive IPO Grants. One-third of the restricted shares subject to the Executive IPO Grants will be vested at grant and the remaining shares will vest in eight quarterly installment beginning three months after effectiveness of this registration statement. We currently expect to issue to Dr. Forbes and Mr. Giroux an aggregate of 435,450 vested restricted shares and 870,898 restricted shares in respect of the Executive IPO Grants on the date the registration statement of which this prospectus forms a part becomes effective or, if later, on the date we file a registration statement on Form S-8 covering the issuance of the shares. 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 Executive IPO Grants. Based on an assumed initial public offering price of $15.00 per ordinary share, which is the midpoint of the price range set forth on the cover page of this prospectus, we expect our tax obligation with respect to the 435,450 vested restricted shares will be $6.5 million.

In connection with this offering 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 | 26,491 | 34,060 | 7.73 | 3/4/2026 | — | — |
| | 9/20/2017 | — | 83,741 | 2.64 | 9/20/2027 | — | — |
| Richard Giroux | 3/4/2016 | 21,418 | 27,538 | 7.73 | 3/4/2026 | — | — |
| | 9/20/2017 | — | 77,299 | 2.64 | 9/20/2027 | — | — |
| Stuart Naylor, Ph.D. | 4/24/2015 | — | — | — | — | 25,669 | 37,220 |
| | 3/4/2016 | 11,272 | 14,494 | 7.73 | 3/4/2026 | — | — |
| | 9/20/2017 | — | 12,883 | 2.64 | 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 Executive IPO Grants 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 shares 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 share 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. | 19,324 |
| Keith R. Harris, Ph.D. | 12,883 |
| Ellen Hukkelhoven, Ph.D. | — |
| Arnold J. Levine, Ph.D. | 6,441 |
| Joel S. Marcus, J.D. | 12,883 |
| Neil Mendoza | 12,883 |

In January 2018, our non-employee directors were granted options to purchase our ordinary shares in the following amounts: Mr. Shenk 23,189, Mr. Harris 23,189, Mr. Mendoza 15,459, Mr. Marcus 15,459 and Mr. Levine 15,459. The options vest in full on the first anniversary of the grant date.

Effective on the effective date of the registration statement of which this prospectus forms a part, we intend to adopt a compensation program for our non-employee directors under which each non-employee director will receive the following amounts for their services on our board of directors:

- an option to purchase 50,000 ordinary shares upon the director’s initial election or appointment to our board of directors that occurs after our initial public offering;
- if the director has served on our board of directors for at least six months as of the date of an annual meeting of shareholders, and will continue to serve as a non-employee director immediately following such meeting, an option to purchase 25,000 ordinary shares on the date of the annual meeting;
- an annual director fee of $25,000; and
- if the director serves on a committee of our board of directors or in the other capacities stated below, an additional annual fee as follows:
  - chairman of the board or lead independent director, $25,000;

- chairman of the audit committee, $15,000;
- audit committee member other than the chairman, $5,000;
- chairman of the compensation committee, $10,000;
- compensation committee member other than the chairman, $5,000;
- chairman of the nominating and corporate governance committee, $10,000; and
- nominating and corporate governance committee member other than the chairman, $5,000.

Options granted to our non-employee directors under the program will have an exercise price equal to the fair market value of our ordinary shares on the date of grant and will expire not later than ten years after the date of grant. The options granted upon a director's initial election or appointment will vest in thirty-six (36) substantially equal monthly installments following the date of grant. The options granted annually to directors will vest in a single installment on the earlier of the day before the next annual meeting or the first anniversary of the date of grant. In addition, all unvested options will vest in full upon the occurrence of a change in control.

Director fees under the program will be payable in arrears in four equal quarterly installments not later than the fifteenth day following the final day of each calendar quarter, provided that the amount of each payment will be prorated for any portion of a quarter that a director is not serving on our board and no fee will be payable in respect of any period prior to the effective date of the registration statement of which this prospectus is a part.

**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 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 1,621,360 ordinary shares for issuance under the 2016 Plan as of May 28, 2018.

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 have adopted and our shareholders have approved 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 3,054,996 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) 4% of the ordinary shares outstanding on the final day of the immediately preceding calendar year and (B) a smaller number of shares determined by our board of directors. No more than 16,547,897 ordinary shares may be issued under the 2018 Plan upon the exercise of incentive stock options. Shares issued under the 2018 Plan may be authorized but unissued shares, shares purchased on the open market or treasury shares.

If an award under the 2018 Plan or the 2016 Plan, expires, lapses or is terminated, exchanged for cash, surrendered, repurchased, canceled without having been fully exercised or forfeited, any unused shares subject to the award will, as applicable, become or again be available for new grants under the 2018 Plan. Awards granted under the 2018 Plan in substitution for any options or other share or share-based awards granted by an entity before the entity's merger or consolidation with us or our acquisition of the entity's property or stock will not reduce the shares available for grant under the 2018 Plan, but will count against the maximum number of shares that may be issued upon the exercise of incentive stock options.

*Awards*

The 2018 Plan provides for the grant of options, including incentive stock options, or ISOs, and nonqualified stock options, or NSOs, share appreciation rights, or SARs, restricted shares, dividend equivalents, restricted share units, or RSUs, and other share or cash based awards. Certain awards under the 2018 Plan may constitute or provide for payment of "nonqualified deferred compensation" under Section 409A of the Code. All awards under the 2018 Plan will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms and post-termination exercise limitations. A brief description of each award type follows.

- *Options and SARs*. Options provide for the purchase of our ordinary shares in the future at an exercise price set on the grant date. ISOs, by contrast to NSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding period and other requirements of the Code are satisfied. SARs entitle their holder, upon exercise, to receive from us an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The plan administrator will determine the number of shares covered by each option and SAR, the exercise price of each option and SAR and the conditions and limitations applicable to the exercise of each option and SAR. The exercise price of an option or SAR will not be less than 100% of the fair market value of the underlying share on the grant date (or 110% in the case of ISOs granted to certain significant shareholders), except with respect to certain substitute awards granted in connection with a corporate transaction. The term of an option or SAR may not be longer than ten years (or five years in the case of ISOs granted to certain significant shareholders).

- *Restricted Shares and RSUs.* A restricted share is an award of nontransferable ordinary shares that remain forfeitable unless and until specified conditions are met and which may be subject to a purchase price. RSUs are contractual promises to deliver ordinary shares in the future, which may also remain forfeitable unless and until specified conditions are met and may be accompanied by the right to receive the equivalent value of dividends paid on ordinary shares prior to the delivery of the underlying shares. The plan administrator may provide that the delivery of the shares underlying RSUs will be deferred on a mandatory basis or at the election of the participant. The terms and conditions applicable to restricted shares and RSUs will be determined by the plan administrator, subject to the conditions and limitations contained in the 2018 Plan.

- *Other Share or Cash Based Awards.* Other share or cash based awards are awards of cash, fully vested ordinary shares and other awards valued wholly or partially by referring to, or otherwise based on, our ordinary shares or other property. Other share or cash based awards may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments and as payment in lieu of compensation to which a participant is otherwise entitled. The plan administrator will determine the terms and conditions of other share or cash based awards, which may include any purchase price, performance goal, transfer restrictions and vesting conditions.

*Performance Criteria*

The plan administrator may select performance criteria for an award to establish performance goals for a performance period. Performance criteria under the 2018 Plan may include, but are not limited to, the following: net earnings or losses (either before or after one or more of interest, taxes, depreciation, amortization, and non-cash equity-based compensation expense); gross or net sales or revenue or sales or revenue growth; net income (either before or after taxes) or adjusted net income; profits (including but not limited to gross profits, net profits, profit growth, net operation profit or economic profit), profit return ratios or operating margin; budget or operating earnings (either before or after taxes or before or after allocation of corporate overhead and bonus); cash flow (including operating cash flow and free cash flow or cash flow return on capital); return on assets; return on capital or invested capital; cost of capital; return on shareholders' equity; total shareholder return; return on sales; costs, reductions in costs and cost control measures; expenses; working capital; earnings or loss per share; adjusted earnings or loss per share; price per share or dividends per share (or appreciation in or maintenance of such price or dividends); regulatory achievements or compliance; implementation, completion or attainment of objectives relating to research, development, regulatory, commercial, or strategic milestones or developments; market share; economic value or economic value added models; division, group or corporate financial goals; customer satisfaction/growth; customer service; employee satisfaction; recruitment and maintenance of personnel; human resources management; supervision of litigation and other legal matters; strategic partnerships and transactions; financial ratios (including those measuring liquidity, activity, profitability or leverage); debt levels or reductions; sales-related goals; financing and other capital raising transactions; cash on hand; acquisition activity; investment sourcing activity; and marketing initiatives, any of which may be measured in absolute terms or as compared to any incremental increase or decrease. Such performance goals also may be based solely by reference to the company's performance or the performance of a subsidiary, division, business segment or business unit of the company or a subsidiary, or based upon performance relative to performance of other companies or upon comparisons of any of the indicators of performance relative to performance of other companies. When determining performance goals, the plan administrator may provide for exclusion of the impact of an event or occurrence which the plan administrator determines should appropriately be excluded, including, without limitation, non-recurring charges or events, acquisitions or divestitures, changes in the corporate or capital structure, events unrelated to the business or outside of the control of management, foreign exchange considerations, and legal, regulatory, tax or accounting changes.

*Certain Transactions*

In connection with certain corporate transactions and events affecting our ordinary shares, including a change in control, or change in any applicable laws or accounting principles, the plan administrator has broad discretion to take action under the 2018 Plan to prevent the dilution or enlargement of intended benefits, facilitate the transaction or event or give effect to the change in applicable laws or accounting principles. This includes canceling awards for cash or property, accelerating the vesting of awards, providing for the assumption or substitution of awards by a successor entity, adjusting the number and type of shares subject to outstanding awards and/or with respect to which awards may be granted under the 2018 Plan and replacing or terminating awards under the 2018 Plan. In addition, in the event of certain non-reciprocal transactions with our shareholders, the plan administrator will make equitable adjustments to the 2018 Plan and outstanding awards as it deems appropriate to reflect the transaction.

*Plan Amendment and Termination*

Our board of directors may amend or terminate the 2018 Plan at any time; however, no amendment, other than an amendment that increases the number of shares available under the 2018 Plan, may materially and adversely affect an award outstanding under the 2018 Plan without the consent of the affected participant and shareholder approval will be obtained for any amendment to the extent necessary to comply with applicable laws. Further, the plan administrator cannot, without the approval of our shareholders, amend any outstanding option or SAR to reduce its price per share. The 2018 Plan will remain in effect until the tenth anniversary of its effective date, unless earlier terminated by our board of directors. No awards may be granted under the 2018 Plan after its termination.

*Non-US Participants, Claw-Back Provisions, Transferability and Participant Payments*

The plan administrator may modify awards granted to participants who are non-US nationals or employed outside the United States or establish subplans or procedures to address differences in laws, rules, regulations or customs of such jurisdictions outside the United States. All awards will be subject to any company claw-back policy as set forth in such claw-back policy or the applicable award agreement. Except as the plan administrator may determine or provide in an award agreement, awards under the 2018 Plan are generally non-transferrable, except by will or the laws of descent and distribution, or, subject to the plan administrator's consent, pursuant to a domestic relations order, and are generally exercisable only by the participant. With regard to tax withholding obligations arising in connection with awards under the 2018 Plan, and exercise price obligations arising in connection with the exercise of options under the 2018 Plan, the plan administrator may, in its discretion, accept cash, wire transfer or check, our ordinary shares that meet specified conditions, a promissory note, a "market sell order," such other consideration as the plan administrator deems suitable or any combination of the foregoing.

***2018 Employee Share Purchase Plan***

Effective the day prior to the first public trading date of our ordinary shares, we have adopted and our shareholders have approved 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 509,166 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 lesser of (A) 1% 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 3,818,745 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 25% 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 25,000 shares. In addition, no employee will be permitted to accrue the right to purchase shares under the 2018 ESPP at a rate in excess of $25,000 worth of shares during any calendar year during which such a purchase right is outstanding (based on the fair market value per share of our ordinary shares as of the first day of the offering period).

On the first trading day of each offering period, each participant will automatically be granted an option to purchase our ordinary shares. The option will expire at the end of the applicable offering period, and will be exercised at that time to the extent of the payroll deductions accumulated during the offering period. The purchase price of the shares, in the absence of a contrary designation, will be 85% of the lower of the fair market value of our ordinary shares on the first trading day of the offering period or on the purchase date. Participants may voluntarily end their participation in the 2018 ESPP at any time at least one week prior to the end of the applicable offering period, and will be paid their accrued payroll deductions that have not yet been used to purchase ordinary shares. Participation ends automatically upon a participant's termination of employment.

A participant may not transfer rights granted under the 2018 ESPP other than by will or the laws of descent and distribution.

*Certain Transactions*

In the event of certain non-reciprocal transactions or events affecting our ordinary shares known as "equity restructurings," the plan administrator will make equitable adjustments to the 2018 ESPP and outstanding rights. In the event of certain unusual or non-recurring events or transactions, including a change in control, the plan administrator may provide for (1) either the replacement of outstanding rights with other rights or property or termination of outstanding rights in exchange for cash, (2) the assumption or substitution of outstanding rights by the successor or survivor corporation or parent or subsidiary thereof, if any, (3) the adjustment in the number and type of shares subject to outstanding rights, (4) the use of participants' accumulated payroll deductions to purchase shares on a new purchase date prior to the next scheduled purchase date and termination of any rights under ongoing offering periods or (5) the termination of all outstanding rights.

*Plan Amendment*

The plan administrator may amend, suspend or terminate the 2018 ESPP at any time. However, shareholder approval will be obtained for any amendment that increases the aggregate number or changes the type of shares that may be sold pursuant to rights under the 2018 ESPP, changes the corporations or classes of corporations whose employees are eligible to participate in the 2018 ESPP or changes the 2018 ESPP in any manner that would cause the 2018 ESPP to no longer be an employee stock purchase plan within the meaning of Section 423(b) of the Code.

## CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following includes a summary of transactions since January 1, 2015 to which we have been a party in which the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our share capital or any member of the immediate family of any of the foregoing persons had, or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under “Executive and Director Compensation.” We also describe below certain other transactions with our directors, executive officers and shareholders.

### Preferred and Ordinary Share Financings

***Series C Preferred Shares***

From October 2015 through April 2018, we issued an aggregate 10,172,835 Series C preferred shares at a purchase price of $10.48 per share, for aggregate consideration of approximately $106.6 million, to investors.

From April 2016 to September 2017, we issued an aggregate 118,526 Series C preferred shares to Kadmon Corporation, LLC, or Kadmon, with an aggregate value of approximately $1.2 million as partial payment of amounts owed under the transition services agreement, or Kadmon TSA. See “—Kadmon Transition Services Agreement” for additional information.

In May 2017, we issued a convertible note to an entity affiliated with Alexandria Equities, No. 7, LLC, or Alexandria, in the principal amount of $2.5 million and an interest rate of 10% per annum, or the Convertible Note. In November 2017, we issued 238,579 Series C preferred shares to Alexandria, with an aggregate value of approximately $2.5 million, upon conversion of the Convertible Note in satisfaction of the full principal. In accordance with the terms of the Convertible Note, the accrued interest in an amount of $0.1 million was cancelled.

***Warrants***

In September 2017, we issued a warrant to Perceptive Life Sciences Master Fund, Ltd., to purchase 695,696 of our Series C preferred shares at an exercise price of $10.48, which was valued under the Black- Scholes pricing model at approximately $1.7 million.

In November 2017, we issued a warrant to Alexandria to purchase 231,898 Series C preferred shares at an exercise price of $10.48, 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 1,050,831 Series A ordinary shares of purchase prices of $7.76 and $13.58 per share, for an aggregate consideration of approximately $8.7 million to investors and an aggregate of 5,611,791 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† | 855,673 | — | — |
| Richard Giroux† | 571,829 | — | — |
| Stuart Naylor | 510,900 | — | — |
| Thomas Shenk | 170,809 | — | — |
| Gregory S. Moss | 41,285 | — | — |
| Joel S. Marcus | 32,208 | 47,714 | — |
| Neil Mendoza | 12,883 | — | — |
| **5% or Greater Shareholders**(1) | — | — | — |
| Kadmon Corporation, LLC | 3,416,181 | 118,526 | — |
| Perceptive Life Sciences Master Fund, Ltd | — | 2,624,369 | 695,696 |
| Adena Estate, Inc. | 322,081 | 1,431,475 | — |
| Alexandria Equities No. 7, LLC | 96,495 | 1,321,000 | 231,898 |
| Robin Ali, Ph.D.† | 1,094,255 | — | — |

(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 |
| Gregory S. Moss | Kadmon Corporation, LLC |
| Ellen Hukkelhoven | Perceptive Life Sciences Master Fund, Ltd |
| Joel S. Marcus | Alexandria Equities No. 7, LLC |

Drs. Forbes and Shenk will resign from the board of directors of Kadmon Holdings, Inc. effective upon the effectiveness of this registration statement of which this prospectus forms a part.

**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 448,157 Series A ordinary shares. Under the terms of the agreement, Dr. Ali will receive aggregate compensation of £110,000 per year, or approximately $146,000 using average exchange rates as of December 31, 2017. The agreement may be terminated at any time by either party by giving twelve-months' notice. For the years ended December 31, 2015, 2016 and 2017, the Company recorded £110,000, £110,000 and £110,000 or approximately $162,000, $135,000 and $128,000, respectively, using the average exchange rates during the year ended December 31, 2015, 2016 and 2017, respectively, in research and development costs under these agreements. Future obligations to be paid under this agreement equal £110,000, or approximately $149,000, using exchange rates as of December 31, 2017.

In April 2015, we entered into a service agreement with Stuart Naylor, one of our officers and directors. On April 24, 2015, we granted Mr. Naylor pursuant to the service agreement 248,969 Series A ordinary shares. For further information, see "Executive and Director Compensation—Executive Compensation Arrangements.

**Consulting Agreement*s***

We and Samuel D. Waksal, Ph.D., a holder of 7.8% of our outstanding equity at the time of our formation in March 2015, and therefore a "related person" under Item 404 of Regulation S-K, entered into a consulting agreement on April 24, 2015 that was subsequently renewed on January 1, 2016, January 1, 2017 and January 1, 2018. Pursuant to the terms of the consulting agreement, we paid Dr. Waksal compensation for his consulting services of $750,000, $850,000 and $850,000 for each of the years ended December 31, 2015, December 31, 2016, and December 31, 2017, respectively. Effective on May 14, 2018, we terminated Dr. Waksal's agreement, and pursuant to its terms, we have agreed to pay him compensation of $197,260 for services performed during 2018. In addition, on March 4, 2016 and September 20, 2017, Dr. Waksal was granted options to purchase 51,533 and 77,299 ordinary shares, respectively, at exercise prices of $7.72 and $2.64, respectively. In 2002, Dr. Waksal was charged by the SEC with violating the federal securities laws in connection with trades made in the shares of ImClone Systems Incorporated, where he served as president and chief executive officer and as a director. Dr. Waksal was also charged with, and subsequently pled guilty to, securities fraud, bank fraud, wire fraud, obstruction of justice, perjury and related conspiracy charges. He is subject to a final judgment and order on consent that permanently bars him from acting as an officer or director of any public company. As of April 30, 2018, Dr. Waksal held shares representing approximately 2.9% of our outstanding equity. Upon completion of this offering, Dr. Waksal will hold shares representing approximately 2.2% 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 170,809 Series A ordinary shares for aggregate consideration of $1.3 million. Under the consulting agreement, such shares are subject to forfeiture ratably over a period of three years if Dr. Shenk does not remain a consultant to us.

**Indications of Interest to Participate in this Offering**

Certain of our existing shareholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering.

**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 investment funds) and executive officer against all expenses such as attorneys' fees, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by the director or executive officer or on his behalf, in connection with such proceeding or any claim, issue or matter therein, if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of our company, and with respect to any criminal proceeding, had no reasonable cause to believe the person's conduct was unlawful. For further information, see "Executive and Director Compensation—Limitations of Liability and Indemnification."

**Share Option and Restricted Share Grants to Executive Officers and Directors**

We have granted share options and restricted shares to our executive officers and certain of our directors as more fully described in the section entitled "Executive and Director Compensation."

**Kadmon Transition Services Agreement**

In April 2015, we entered into the Kadmon TSA to provide us with office and laboratory facilities, as well as personal support activities. Under the agreement, we are charged for (i) rent based upon the square footage of the office and laboratory facilities we use, (ii) other personnel support activities based upon hours of the personnel providing the support activities, and (iii) other direct costs incurred by Kadmon on our behalf, plus a 7% administrative fee. We made cash payments under the agreement of $225,078 and $275,941 during the years ended December 31, 2016 and 2017, respectively. During the three-month periods ended March 31, 2017 and 2018, we made cash payments to Kadmon totaling $275,941 and $997,417, respectively. From April 2016 to September 2017, we issued an aggregate 118,526 Series C preferred shares to Kadmon in aggregate amount of $1,242,000 as partial payment of amounts owed under the agreement. As of December 31, 2016 and 2017 and March 31, 2018, the amount due to Kadmon was $543,038, $861,030 and $6,493, respectively. Either party may terminate the agreement upon 30-days' notice. The Kadmon TSA terminated on April 24, 2018.

**Moorfields Lease**

In February 2016, we entered into a five-year lease with Moorfields Eye Hospital, NHS Foundation Trust and Kadmon, a greater than 5% shareholder. Under the lease, Kadmon is a guarantor of our rent obligations and has agreed to indemnify Moorfields as the landlord against any failure by the tenant to pay the rent or otherwise perform its obligations thereunder.

**UCL Agreements**

***Services Agreement***

In October 2016, we entered into a four-year services agreement with UCL Consultants Limited, an entity affiliated with UCLB. One of our shareholders, Robin Ali, is a professor at University College London, or UCL, an entity affiliated with UCLB and UCL Consultants Limited. Under the agreement, UCL Consultants Limited provides pre-clinical research and development services under our direction. In connection with the agreement, we issued several work orders during the years ended December 31, 2016 and 2017 in aggregate amounts of $1,574,000 and $311,000, respectively. The total research and development expenses for the years ended December 31, 2016 and 2017 were approximately $278,000 and $538,000, respectively. Future obligations under the agreement are approximately $1,438,869. As of the years ended December 31, 2016 and 2017, the amount due to UCL was $251,754 and $775,315, respectively. Either party may terminate the agreement upon 30-days written notice.

***Manufacturing and Supply Agreement***

In September 2016, we entered into a manufacturing and drug supply agreement with UCL to manufacture materials for our clinical trials under our direction, which was terminated in January 2018. The total research and development expenses for the years ending December 31, 2016 and 2017 were $456,106 and $1,904,352, respectively. As of the years ended December 31, 2016 and 2017, the amount due to UCL was $412,395 and $2,466,142, respectively.

**ARE Leases**

***July 2016 Lease***

Effective July 2016, we entered into a non-cancellable operating lease for laboratory facilities in New York with ARE-East River Science Park, LLC, or ARE, an entity affiliated with Alexandria and Joel S. Marcus, Executive Chairman of Alexandria Real Estate Equities, Inc. Under the lease, we pay monthly base rent, property management fees and operating expenses for the duration of the lease term, which expires in December 2021. The total rent expense under the lease for the years ended December 31, 2016 and 2017 was $243,780 and $487,559, respectively. In July 2016, in connection with the signing of the lease, we entered into a standby letter of credit agreement for $122,866, which serves as a security deposit for the premises. The standby letter of credit expires on is automatically renewed annually through July 7, 2021. As of the years ended December 31, 2016 and 2017, the balance of deferred rent was $243,780 and $231,276, respectively. Aggregate future minimum rental payments under the lease are $2,181,520 as of December 31, 2017.

***December 2016 Lease***

In December 2016, we entered into a non-cancellable operating lease for laboratory and office facilities in New York with ARE expiring in October 2032. Under the lease, we pay monthly base rent, property management fees, and operating expenses during the lease term. In December 2016, in connection with the signing of the lease, we entered into a standby letter of credit agreement for $321,977, which served as a security deposit for the premises. The standby letter of credit was cancelled on November 2017. In October 2017, the lease was amended whereby the lease would terminate on March 2018 and only base rent and management fees in the aggregate amount of $563,507 would be due for the period from November 2017 through March 2018. Under the amendment, we issued a promissory note in the principal amount of $1,442,009 to ARE at an interest rate of 5% per annum, which removed the balance of the deferred rent and accrued the future rent payments. The note is due on December 31, 2018, however, the note and accrued interest will become due and payable if we achieve sufficient liquidity as defined in the note. If we do not have sufficient liquidity, which is defined as our cash, cash equivalents and liquid short-term investments of at least an investment grade are at least 20 times greater than the note plus accrued interest, prior to the due date, we may repay the note in either cash or Series C preferred shares. We recorded an interest expense in the amount of $13,037 for the year ended December 31, 2017. The total rent expense under the operating lease was $43,578 and $1,660,806 for the years ended December 31, 2016 and 2017 respectively. As of the years ended December 31, 2016 and 2017, the balance of deferred lease obligation was $11,380 and $0 respectively. Aggregate future minimal rental payments under the lease are $332,442 as of December 31, 2017.

**Shareholder Agreement**

Upon consummation of the Corporate Reorganization, we will enter into a Shareholder Agreement with our shareholders, including Alexandria Forbes, Richard Giroux, Stuart Naylor, Joel S. Marcus, Thomas Shenk, Keith Harris, Arnold Levine, Kadmon Corporation, LLC, Perceptive Life Sciences Master Fund, Ltd., Adena Estate, Inc., Alexandria Equities No. 7, LLC. and Robin Ali. The Shareholder Agreement, other than provisions related to registration rights, confidentiality, rights of third parties and governing law, will terminate upon consummation of our initial public offering. Provisions related to registration rights will terminate upon the earlier to occur of a deemed liquidation event, such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of a holder's shares without limitation during a three-month period without registration, and the third anniversary of our initial public offering. See "Description of Share Capital and Articles of Association-Registration Rights" for additional information.

**Policies and Procedures for Related Person Transactions**

Our board of directors has adopted a written related person transaction policy, to be effective upon the closing of this offering, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, where the amount involved exceeds $5,000 in any fiscal year and a related person had, has or will have a direct or indirect material interest, including without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

## PRINCIPAL SHAREHOLDERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares, as of April 30, 2018, (i) immediately prior to this offering, and (ii) after giving effect to the offering:

- 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 27,184,140 ordinary shares outstanding as of April 30, 2018, after giving effect to our Corporate Reorganization, the conversion of the preferred shares, including preferred shares issued in connection with the exercise of warrants, into ordinary shares prior to the closing of this offering, and, solely in the case of beneficial ownership after giving effect to the offering, the Executive IPO Grants. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, ordinary shares subject to options, warrants or other rights held by such person that are currently exercisable or will become exercisable within 60 days of April 30, 2018 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless noted otherwise, the address of all listed shareholders is 430 E. 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.

Certain of our existing shareholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The following table does not reflect any potential purchases by these potential purchasers. If any shares are purchased by our existing shareholders or their affiliated entities, the number and percentage of ordinary shares beneficially owned by them after this offering will differ from those set forth in the following table.

| | 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) | 3,534,707 | 16.9% | 3,534,707 | 13.0% |
| Perceptive Life Sciences Master Fund, Ltd(2) | 3,320,065 | 15.9 | 3,320,065 | 12.2 |
| Adena Estate, Inc.(3) | 1,753,556 | 8.4 | 1,753,556 | 6.5 |
| Alexandria Equities No. 7, LLC(4) | 1,649,393 | 7.9 | 1,649,393 | 6.1 |
| Robin Ali, Ph.D. | 1,094,255 | 5.2 | 1,094,255 | 4.0 |
| ***Named Executive Officers and Directors*** | | | | |
| Keith R. Harris, Ph.D.(5) | 12,883 | * | 12,883 | * |
| Alexandria Forbes, Ph.D.(6) | 889,714 | 4.3 | 1,542,888 | 5.7 |
| Ellen Hukkelhoven, Ph.D. | — | — | — | — |
| Arnold J. Levine, Ph.D.(7) | 6,441 | * | 6,441 | * |
| Joel S. Marcus(8) | 1,742,198 | 8.3 | 1,742,198 | 6.4 |
| Neil Mendoza(9) | 25,766 | * | 25,766 | * |
| Gregory S. Moss | 41,285 | * | 41,285 | * |
| Stuart Naylor, Ph.D.(10) | 512,509 | 2.5 | 512,509 | 1.9 |
| Thomas E. Shenk, Ph.D.(11) | 190,133 | * | 190,133 | * |
| Richard Giroux(12) | 599,366 | 2.9 | 1,252,540 | 4.6 |
| All executive officers and directors as a group (10 persons)(13) | 4,020,295 | 19.1 | 5,326,643 | 19.5 |

* 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. and Gregory S. Moss, one of our directors, is Senior Vice President, Deputy General Counsel of Kadmon Holdings, Inc. Drs. Forbes and Shenk will resign from the board of directors of Kadmon Holdings, Inc. effective upon the effectiveness of this registration statement. The address of Kadmon Corporation, LLC is 450 E. 29th Street, 16th Floor, New York, New York 10016.

(2) Includes a warrant to purchase 695,696 ordinary shares that is or will be immediately exercisable within 60 days of April 30, 2018 held by Perceptive Life Sciences Master Fund, Ltd. Ellen Hukkelhoven, one of our directors, is a senior analyst at Perceptive Advisors, LLC, which is the investment manager of Perceptive Life Sciences Master Fund, Ltd. 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) The address of Adena Estate, Inc. is Craigmuir Chambers, P.O. Box 71, Road Town, Tortola, VG1110, British Virgin Islands.

(4) Includes a warrant to purchase 231,898 ordinary shares. The address for Alexandria Equities No. 7, LLC is 385 E. Colorado Blvd., Suite 299, Pasadena, California 91101. One of our directors, Joel S. Marcus, is the Executive Chairman of ARE-QRS Corp., the general partner of Alexandria Real Estate Equities L.P., which is the managing member of ARE-Special Services, LLC, which is the managing member of Alexandria Equities No. 7, LLC.

(5) Consists of options to purchase 12,883 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.

(6) Consists of 855,673 ordinary shares and options to purchase 34,041 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018. In addition, shares beneficially owned after offering reflects 217,725 vested shares and 435,449 unvested shares granted upon effectiveness of this registration statement as part of the Execution IPO Grants.

(7) Consists of options to purchase 6,441 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.

(8) Includes a warrant to purchase 231,898 ordinary shares held by Alexandria Equities No. 7, LLC, 79,922 ordinary shares held by Third Amended and Restated Joel and Barbara Marcus Family Trust and options held by Joel S. Marcus to purchase 12,883 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018. Joel Marcus, one of our directors, is the Executive Chairman of ARE-QRS Corp., the general partner of Alexandria Real Estate Equities L.P., which is the managing member of ARE-Special Services, LLC, which is the managing member of Alexandria Equities No. 7, LLC. ARE-QRS Corp. has full voting and investment power with respect to the shares owned by Alexandria Equities No. 7, LLC. As Executive Chairman of ARE-QRS Corp., Mr. Marcus may be deemed to have voting and investment power with respect to the shares owned by Alexandria Equities No. 7, LLC. Mr. Marcus disclaims beneficial ownership of the shares held by Alexandria Equities No. 7, LLC, except to the extent of his underlying pecuniary interest therein.

(9) Includes options to purchase 12,883 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.

(10) Includes options to purchase 14,492 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.

(11) Consists of 170,809 ordinary shares held by Double Epiphany, LLC and options held by Thomas Shenk to purchase 19,324 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018. The managing members of Double Epiphany, LLC are Thomas E. Shenk and Lillian W. Chiang, who have full voting and investment power with respect to the shares held by Double Epiphany, LLC. The address for Double Epiphany, LLC is 12 Boudinot Street, Princeton, New Jersey 08540.

(12) Includes options to purchase 27,537 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018. In addition, shares beneficially owned after offering reflects 217,725 vested shares granted and 435,449 unvested shares granted upon effectiveness of this registration statement as part of the Execution IPO Grants.

(13) Includes a warrant to purchase 231,898 ordinary shares and options to purchase 140,484 ordinary shares that are or will be immediately exercisable within 60 days of April 30, 2018.

## DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

*The following describes the issued share capital of MeiraGTx Holdings plc (the "Issuer"), summarizes the material provisions of the articles of association of the Issuer as are anticipated to be in effect upon the completion of this offering and highlights certain differences in corporate law in the Cayman Islands and Delaware, the United States. In this "Description of Share Capital and Articles of Association" discussion, we use the term "we," "us" and "our" to refer to the Issuer.*

### General

We were incorporated pursuant to the laws of the Cayman Islands as an exempted company with limited liability to become the holding company of our business. Pursuant to the terms of our corporate reorganization, which will be completed prior to the completion of this offering, all of the issued share capital in MeiraGTx Limited will be exchanged for shares in the Issuer and, as a result, MeiraGTx Limited will become a wholly owned subsidiary of the Issuer. See "Corporate Reorganization" for more information.

The principal legislation under which the Issuer will operate and its shares will be issued is the Cayman Islands Companies Law (2018 Revision) (the "Companies Law").

Our register of shareholders will be maintained by Computershare Trust Company N.A.

Following our Corporate Reorganization, certain resolutions will be required to be passed by our shareholders prior to the completion of this offering. These will include resolutions for the:

- adoption of new articles of association that will become effective upon the completion of this offering; and
- reorganization of the share capital of the Issuer.

### Share Capital

Upon completion of the Corporate Reorganization, the conversion of the preferred shares into ordinary shares, including preferred shares issued in connection with the exercise of warrants, and the effectiveness of a 1 for 3.881 reverse share split (by way of consolidation of the share capital of the Company), the authorized share capital of MeiraGTx Holdings plc will consist of $50,000 divided into 1,288,327,750 shares, nominal value $0.00003881 per share. Upon completion of the Corporate Reorganization, the conversion of the preferred shares into ordinary shares, including preferred shares issued in connection with the exercise of warrants, the effectiveness of a 1 for 3.881 reverse share split (by way of consolidation of the share capital of the Company), and the issuance of the Executive IPO Grants, there will be 22,184,140 ordinary shares issued and outstanding. As of April 30, 2018, after giving effect to the Corporate Reorganization, the exercise of all outstanding warrants, and the conversion of the preferred shares into ordinary shares, there were 74 holders of record.

### Ordinary Shares

#### *General*

All of our issued and outstanding ordinary shares are fully paid and non assessable. Certificates representing our issued and outstanding ordinary shares are generally not issued and legal title to our issued shares is recorded in registered form in the register of members. Holders of our ordinary shares have no preemptive, subscription, redemption or conversion rights.

Our board of directors may provide for other classes of shares, including classes of preferred shares, out of our authorized but unissued share capital, which could be utilized for a variety of corporate purposes, including future offerings to raise capital for corporate purposes or for use in employee benefit plans. Such additional classes of shares shall have such rights, restrictions, preferences, privileges and payment obligations as determined by our board of directors. If we issue any preferred shares, the rights, preferences and privileges of holders of our ordinary shares will be subject to, and may be adversely affected by, the rights of the holders of such preferred shares. See "—Variation of rights."

**Dividends**

The holders of our ordinary shares are entitled to such dividends as may be declared by our board of directors subject to the Companies Law and our amended and restated memorandum and articles of association. Dividends and other distributions on issued and outstanding ordinary shares may be paid out of the funds of the Issuer lawfully available for such purpose, subject to any preference of any outstanding preferred shares. Dividends and other distributions will be distributed among the holders of our ordinary shares on a pro rata basis.

***Voting rights***

Voting at any shareholders' meeting is by show of hands, unless voting by way of poll demanded by the chairman of the board of directors or any shareholder present or voting by proxy. On a show of hands every shareholder present in person or by proxy shall have one vote and on a poll every shareholder present in person or by proxy shall have one vote for each ordinary share on all matters upon which the ordinary shares are entitled to vote.

A quorum required for a meeting of shareholders consists of holders with at least one-third of the votes eligible to be cast at any such general meeting of the Issuer.

An ordinary resolution to be passed by the shareholders requires the affirmative vote of a simple majority of the votes attaching to the ordinary shares cast in a general meeting, while a special resolution requires the affirmative vote of not less than two thirds of the votes attaching to the ordinary shares cast in a general meeting. An ordinary resolution or a special resolution may also be adopted by way of unanimous written resolution signed by or on behalf of each shareholder who would have been entitled to vote on such matter at a general meeting without a meeting being held. A special resolution will be required for matters such as certain merger or consolidation transactions, the change of name of the Issuer, making changes to our amended and restated memorandum and articles of association, or the voluntary winding up of the Issuer.

***Variation of rights***

The rights attached to any class of shares (unless otherwise provided by the terms of issue of that class), such as voting, dividends and the like, may be varied only with the sanction of a resolution passed by not less than two-thirds of the votes attaching to the shares of the relevant class cast in a meeting of the holders of the shares of that class, or by the written consent of the holders of not less than two-thirds of the shares of that class. The rights conferred upon the holders of the shares of any class shall not (unless otherwise provided by the terms of issue of that class) be deemed to be varied by the creation or issue of further shares ranking in priority to or pari passu with such previously existing shares.

***Transfer of ordinary shares***

Any of our shareholders may transfer all or any of his or her ordinary shares by an instrument of transfer in the usual or common form or any other form approved by our board of directors, subject to the applicable restrictions of our amended and restated memorandum and articles of association which will become effective upon the completion of this offering, such as the suspension of transfers for a period immediately preceding a general meeting, or the determination that a proposed transfer is not eligible.

***Liquidation***

On a return of capital on winding up or otherwise (other than on conversion, redemption or purchase of ordinary shares), assets available for distribution among the holders of ordinary shares shall be distributed among the holders of the ordinary shares on a pro rata basis.

***Directors***

The management of our company is vested in our board of directors. The quorum necessary for any meeting of our board of directors shall consist of at least a majority of the members of our board of directors and questions arising at any meeting shall be decided by a majority of votes.

Our amended and restated memorandum and articles of association, which will become effective upon completion of this offering, provide that our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of shareholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. The election of directors shall be by a plurality of the votes of the shares entitled to vote on the election of directors.

In addition, subject to the maximum number of directors designated by resolution of the board of directors, additional directors may be appointed from time to time by the board of Directors or by ordinary resolution either as a result of a casual vacancy or as an additional director.

Directors may be removed or replaced by an ordinary resolution of the shareholders.

***Indemnity of directors and officers***

Our amended and restated memorandum and articles of association provide that our board of directors and officers shall be indemnified from and against all liability which they incur in execution of their duty in their respective offices, except liability incurred by reason of such director’s or officer’s dishonesty, willful default or fraud.

**Registration Rights**

Holders of Series C preferred shares, as of the effectiveness of the Corporate Reorganization, who hold not less than 3% of the fully diluted share capital of the Company, and certain other holders will be entitled to certain rights with respect to the registration of ordinary shares for public resale under the Securities Act, pursuant to a Shareholder Agreement by and among us and certain of our shareholders. After giving effect to the conversion of the preferred shares into ordinary shares, holders of an aggregate of 16,123,234 ordinary shares will have these rights. These rights terminate upon the earlier to occur of a deemed liquidation event, such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of a holder’s shares without limitation during a three-month period without registration, and the third anniversary of our initial public offering. The registration of ordinary shares as a result of these rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

Subject to certain exceptions, including this offering, if we propose to register any of our ordinary shares in connection with a public offering of such securities solely for cash, we are obligated to notify the eligible holders of such registration. Upon the request of any such eligible holders given within 20 days following the registration notice, we are obligated, subject to certain exceptions, to register all of the ordinary shares then owned by the eligible holder that such holder has requested to be included in such registration. If the holders requesting registration intend to distribute their shares by means of an underwriting, the underwriters of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

**Differences in Corporate Law**

Cayman Islands companies are governed by the Companies Law. The Companies Law is modeled on English law but does not follow recent English Law statutory enactments, and differs from laws applicable to United States corporations and their shareholders. Set forth below is a summary of some significant differences between the provisions of the Companies Law applicable to us and, for comparison purposes, the laws applicable to companies incorporated in the State of Delaware and their shareholders.

***Mergers and similar arrangements***

The Companies Law allows for the merger of two or more companies into either one consolidated company or one or more company(ies) merged into another so as to form a single surviving company. The merger or consolidation of two or more companies under Cayman Islands law requires the directors of the companies to enter into and to approve a written plan of merger or consolidation, which must also be authorized by a special resolution of each constituent company, in which regard see "— Ordinary Shares — Voting Rights" above, and such other authorization, if any, as may be specified in such companies' articles of association. In relation to any merger or consolidation under the Companies Law, dissenting shareholders have certain limited appraisal rights in circumstances which are similar to those available to dissenting shareholders of a Delaware corporation, providing rights to receive payment in cash for the judicially determined fair value of the shares. Appraisal rights are ordinarily available where the consideration offered under the merger is payable in cash or, in some instances, the unlisted securities of a third party.

The Companies Law also includes statutory provisions that facilitate the reconstruction and amalgamation of companies, provided that such a scheme of arrangement is approved by shareholders or creditors who represent a majority in number and 75% in value of each such class of shareholders or creditors who attend and vote, either in person or by proxy, at a meeting or meetings convened for that purpose. The convening of meetings to consider any such scheme of arrangement, and the implementation of the scheme, must be sanctioned by the Grand Court of the Cayman Islands. While a dissenting shareholder has the right to express to the court the view that the transaction ought not to be approved, the court can be expected to approve the arrangement if it determines that:

- the statutory provisions as to the dual majority vote have been met;
- the shareholders have been fairly represented at the meeting in question and the classes properly delineated;
- the arrangement is such that a businessman would reasonably approve; and
- the arrangement is not one that would more properly be sanctioned under some other provision of the Companies Law.

If a scheme of arrangement is thus approved, the dissenting shareholders would have no rights comparable to appraisal rights, which would otherwise ordinarily be available to dissenting shareholders of a Delaware corporation.

When a tender offer to acquire shares is made and accepted (within four months) by holders of not less than 90% of the shares subject to such offer, the offeror may, within a two-month period following the expiration of the initial four month period, require the holders of the remaining shares to transfer such shares on the terms of the offer. An objection can be made to the Grand Court of the Cayman Islands but this is unlikely to succeed unless there is evidence of fraud, bad faith, collusion or inequitable treatment of shareholders.

***Shareholders' suits***

We are not aware of any reported class action having been brought in a Cayman Islands court. Derivative actions have been brought in the Cayman Islands courts, and the Cayman Islands courts have confirmed the availability for such actions. In principle, we will normally be the proper plaintiff and a derivative action may not be brought by a shareholder. However, based on English authorities, which would in all likelihood be of persuasive authority in the Cayman Islands, there are exceptions to the foregoing principle, including when:

- a company acts or proposes to act illegally or ultra vires (beyond the scope of its authority);
- the act complained of, although not ultra vires, could be effected if duly authorized by a special resolution that has not been obtained; and

- those who control the company are perpetrating a "fraud on the minority."

***Fiduciary duties of directors***

Under Delaware corporate law, a director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components, the duty of care and the duty of loyalty. The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director must act in a manner he or she reasonably believes to be in the best interests of the corporation. A director must not use his or her corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interests of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Should such evidence be presented concerning a transaction by a director, the director must prove the procedural fairness of the transaction and that the transaction was of fair value to the corporation.

As a matter of Cayman Islands law, a director of a Cayman Islands company is in the position of a fiduciary with respect to the company and therefore it is considered that he owes the following duties to the company: a duty to act in good faith and in what he considers to be in the best interests of the company; a duty not to make a profit out of his position as director (unless the company permits him to do so); a duty to exercise his powers for the purposes for which they are conferred; and a duty not to put himself in a position where the interests of the company conflict with his personal interest or his duty to a third party. A director of a Cayman Islands company owes to the company a duty to act with skill and care. A director will need to exhibit in the performance of his duties both the degree of skill than may reasonably be expected from a subjective perspective determined by reference to his knowledge and experience and the skill and care objectively to be expected from a person occupying office as a director of the company.

Under our amended and restated memorandum and articles of association, directors who are in any way, whether directly or indirectly, interested in a contract or proposed contract with our company must declare the nature of their interest at a meeting of the board of directors. Following such declaration, a director may vote in respect of any contract or proposed contract notwithstanding his interest; provided that, in exercising any such vote, such director's duties remain as described above.

***Written consent of shareholders***

Under Delaware corporate law, unless otherwise provided in the certificate of incorporation, any action to be taken at any annual or special meeting of shareholders of a corporation may be taken by written consent of the holders of outstanding stock having not less than the minimum number of votes that would be necessary to take that action at a meeting at which all shareholders entitled to vote were present and voted. In addition, a corporation may eliminate the right of shareholders to act by written consent through amendment to its certificate of incorporation.

Cayman Islands law and our amended and restated memorandum and articles of association provide that shareholders may adopt an ordinary resolution or a special resolution by way of unanimous written resolution signed by or on behalf of each shareholder who would have been entitled to vote on such matter at a general meeting without a meeting being held.

***Shareholder proposals***

Under Delaware corporate law, a shareholder has the right to put any proposal before the shareholders at the annual meeting, provided that such shareholder complies with the notice provisions in the governing documents. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings.

Under the laws of the Cayman Islands, a shareholder can only put a proposal before the shareholders at any general meeting in respect of any matter requiring a special resolution if it is set out in the notice calling the meeting. There is no right to introduce new business in respect of any matter requiring a special resolution at any meeting. A general meeting may be called by the board of directors or any other person authorized to do so in the articles of association, but shareholders may be precluded from calling general meetings. Under our amended and restated memorandum and articles of association general meetings shall also be convened on the requisition in writing of any shareholder or shareholders entitled to attend and vote at general meetings of the company and to exercise at least a majority of the voting power permitted to be exercised at any such meeting, deposited at the office specifying the objects of the meeting for a date no later than 21 days from the date of deposit of the requisition signed by such shareholders, and if the directors do not convene such meeting for a date not later than 45 days after the date of such deposit, such shareholders themselves may convene the general meeting in the same manner, as nearly as possible, as that in which general meetings may be convened by the directors, and all reasonable expenses incurred by such shareholders as a result of the failure of the directors to convene the general meeting shall be reimbursed to them by the company. As an exempted Cayman Islands company, we are not obliged by law to call shareholders' annual general meetings.

Under Delaware corporate law, a corporation is required to set a minimum quorum of one-third of the issued and outstanding shares for a shareholders meeting. Cayman Islands law permits a company's articles to have any quorum. See "— Ordinary Shares — Voting Rights."

***Cumulative voting***

Under Delaware corporate law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation specifically provides for it. Cumulative voting potentially facilitates the representation of minority shareholders on a board of directors since it permits a minority shareholder to cast all the votes to which such shareholder is entitled on a single director, which increases such shareholder's voting power with respect to electing such director.

There are no prohibitions in relation to cumulative voting under the laws of the Cayman Islands, but our amended and restated memorandum and articles of association do not provide for cumulative voting. As a result, our shareholders are not afforded any less protection or fewer rights on this issue than shareholders of a Delaware corporation.

***Election and removal of directors***

Under Delaware corporate law, unless otherwise specified in the certificate of incorporation or bylaws of a corporation, directors are elected by a plurality of the votes of the shares entitled to vote on the election of directors and may be removed with or without cause (or, with respect to a classified board, only with cause unless the certificate of incorporation provides otherwise) by the approval of a majority of the outstanding shares entitled to vote.

Similarly, as permitted by the Companies Law and pursuant to our amended and restated memorandum and articles of association, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of shareholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. The election of directors shall be by a plurality of the votes of the shares entitled to vote on the election of directors.

In addition, subject to the maximum number of directors designated by resolution of the board of directors, additional directors may be appointed from time to time by the board of Directors or by ordinary resolution either as a result of a casual vacancy or as an additional director.

Directors may be removed or replaced by an ordinary resolution of the shareholders.

***Written consent of directors***

Under Delaware corporate law, a written consent of the directors must be unanimous to take effect. The position under our amended and restated memorandum and articles of association is the same in this regard.

***Indemnification of directors and executive officers and limitation of liability***

Cayman Islands law does not limit the extent to which a company's amended and restated memorandum and articles of association may provide for indemnification of officers and directors, except to the extent any such provision may be held by the Cayman Islands courts to be contrary to public policy, such as to provide indemnification against civil fraud or the consequences of committing a crime. Our amended and restated memorandum and articles of association, which will become effective upon the completion of this offering, provide that our board of directors and officers shall be indemnified from and against all liability which they incur in execution of their duty in their respective offices, except liability incurred by reason of such directors' or officers' dishonesty, willful default or fraud. This standard of conduct is generally the same as permitted under Delaware corporate law.

***Enforcement of civil liabilities***

The Cayman Islands has a less developed body of securities laws as compared to the United States and provides less protection to investors. Additionally, Cayman Islands companies may not have standing to sue before the Federal courts of the United States. Although there is no statutory enforcement in the Cayman Islands of judgments obtained in the United States, the courts of the Cayman Islands will recognize a foreign judgment as the basis for a claim at common law in the Cayman Islands provided such judgment:

- is one in respect of which the foreign court had jurisdiction over the defendant according to Cayman Islands conflict of law rules;
- is final and conclusive;
- is either for a liquidated sum not in respect of penalties or taxes or a fine or similar fiscal or revenue obligations or, in certain circumstances, for *in personam* non-money relief; and
- was neither obtained in a manner, nor is of a kind enforcement of which is contrary to natural justice or the public policy of the Cayman Islands.

As a result of English case law, which will likely be highly persuasive in the Cayman Islands, the Cayman Islands Courts may also have discretion to enforce judgments obtained in foreign bankruptcy proceedings in other circumstances.

***Anti-money laundering — Cayman Islands***

In order to comply with legislation or regulations aimed at the prevention of money laundering, we are required to adopt and maintain anti-money laundering procedures, and may require subscribers to provide evidence to verify their identity and source of funds. Where permitted, and subject to certain conditions, we may also delegate the maintenance of our anti-money laundering procedures (including the acquisition of due diligence information) to a suitable person.

We reserve the right to request such information as is necessary to verify the identity of a subscriber. In the event of delay or failure on the part of the subscriber in producing any information required for verification purposes, we may refuse to accept the application, in which case any funds received will be returned without interest to the account from which they were originally debited.

We also reserve the right to refuse to make any distribution payment to a shareholder if our directors or officers suspect or are advised that the payment of such distribution to such shareholder might result in a breach of applicable anti-money laundering or other laws or regulations by any person in any relevant jurisdiction, or if such refusal is considered necessary or appropriate to ensure our compliance with any such laws or regulations in any applicable jurisdiction.

If any person resident in the Cayman Islands knows or suspects or has reason for knowing or suspecting that another person is engaged in criminal conduct or is involved with terrorism or terrorist property and the information for that knowledge or suspicion came to their attention in the course of their business in the regulated sector, or other trade, profession, business or employment, the person will be required to report such knowledge or suspicion to (i) the Financial Reporting Authority of the Cayman Islands, pursuant to the Proceeds of Crime Law (2018 Revision) if the disclosure relates to criminal conduct or (ii) to a police officer of the rank of constable or higher, or the Financial Reporting Authority, pursuant to the Terrorism Law (2018 Revision) if the disclosure relates to involvement with terrorism or terrorist financing and property. Such a report shall not be treated as a breach of confidence or of any restriction upon the disclosure of information imposed by any enactment or otherwise.

***Variation of rights of shares***

Under Delaware corporate law, a corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise.

Under Cayman Islands law and our amended and restated memorandum and articles of association, if our share capital is divided into more than one class of shares, we may vary the rights attached to any class with the sanction of a resolution passed by not less than two-thirds of the votes attaching to the shares of the relevant class cast in a meeting of the holders of the shares of that class, or by the written consent of the holders of not less than two-thirds of the shares of that class.

***Sale of assets***

Under Delaware corporate law, a vote of the shareholders is required to approve a sale of assets only when all or substantially all assets are being sold to a person other than a subsidiary of the company.

The Companies Law contains no specific restrictions on the powers of directors to dispose of assets of a company. As a matter of general law, in the exercise of those powers, the directors must discharge their duties of care and to act in good faith, for a proper purpose and in the interests of the company.

***Transactions with interested shareholders***

The Delaware General Corporation Law contains a business combination statute applicable to Delaware corporations whereby, unless the corporation has specifically elected not to be governed by such statute by amendment to its certificate of incorporation, it is prohibited from engaging in certain business combinations with an “interested shareholder” for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or a group who or which owns or owned 15% or more of the target’s outstanding voting stock within the past three years.

This has the effect of limiting the ability of a potential acquirer to make a two-tiered bid for the target in which all shareholders would not be treated equally. The statute does not apply if, among other things, prior to the date on which such shareholder becomes an interested shareholder, the board of directors approves either the business combination or the transaction which resulted in the person becoming an interested shareholder. This encourages any potential acquirer of a Delaware corporation to negotiate the terms of any acquisition transaction with the target’s board of directors.

Cayman Islands law has no comparable statute. As a result, we cannot avail ourselves of the types of protections afforded by the Delaware business combination statute. However, although Cayman Islands law does not regulate transactions between a company and its significant shareholders, it does provide that such transactions must be entered into bona fide in the best interests of the company and not with the effect of constituting a fraud on the minority shareholders.

***Rights of non-resident or foreign shareholders***

There are no limitations imposed by our amended and restated memorandum and articles of association on the rights of non-resident or foreign shareholders to hold or exercise voting rights on our shares. As similarly provided under Delaware corporate law, there are no restrictions on foreign or non-resident ownership or management of a Cayman Islands exempted company under Cayman Islands law. In addition, there are no provisions in our amended and restated memorandum and articles of association governing the ownership threshold above which shareholder ownership must be disclosed.

***Dissolution and winding up***

Under the Delaware General Corporation Law, unless the board of directors approves the proposal to dissolve, dissolution must be approved by shareholders holding 100% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with a dissolution initiated by the board of directors. Under the Companies Law of the Cayman Islands and our amended and restated memorandum and articles of association, our company may be voluntarily dissolved, liquidated or wound up only by a special resolution of our shareholders, in which regard see "— Ordinary Shares — Voting Rights" above. In addition, a company may be wound up by the Grand Court of the Cayman Islands if the company is unable to pay its debts or if the court is of the opinion that it is just and equitable that our company is wound up.

***Inspection of books and records***

Under Delaware corporate law, any shareholder of a corporation may for any proper purpose inspect or make copies of the corporation's stock ledger, list of shareholders and other books and records.

Our shareholders will have no general right under Cayman Islands law to inspect or obtain copies of our list of shareholders or corporate records except our memorandum and restated articles of association.

***Amendment of governing documents***

Under Delaware corporate law, a corporation's certificate of incorporation may be amended only if adopted and declared advisable by the board of directors and approved by a majority of the outstanding shares entitled to vote, and the bylaws may be amended with the approval of a majority of the outstanding shares entitled to vote and may, if so provided in the certificate of incorporation, also be amended by the board of directors. As permitted by Cayman Islands law, our amended and restated memorandum and articles of association may be amended with the sanction of a special resolution of shareholders.

**Transfer Agent and Registrar**

The transfer agent and registrar for our ordinary shares will be Computershare Trust Company, N.A.

**Stock Exchange Listing**

Our ordinary shares have been approved for listing on the Nasdaq Global Select Market under the symbol "MGTX."

# SHARES ELIGIBLE FOR FUTURE SALE

Immediately prior to this offering, there was no public market for our ordinary shares. Future sales of substantial amounts of ordinary shares in the public market, or the perception that such sales may occur, could adversely affect the market price of our ordinary shares.

Upon the closing of this offering, we will have outstanding an aggregate of 27,184,140 ordinary shares, assuming the issuance of 5,000,000 ordinary shares offered by us in this offering (or 27,934,140 ordinary shares if the underwriters exercise their option to purchase 750,000 additional shares in full), and no exercise of options after April 30, 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 22,184,140 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 22,184,140 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 1,614,403 ordinary shares that were subject to share options outstanding as of April 30, 2018, options to purchase 249,158 ordinary shares were vested as of April 30, 2018 and, upon exercise, these shares will be eligible for sale subject to the lock–up agreements described below and Rules 144 and 701 under the Securities Act.

## Lock-up Agreements

We and each of our directors and executive officers and holders of substantially all of our outstanding ordinary shares have agreed that, without the prior written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Barclays Capital Inc., we and they will not, subject to certain exceptions, during the period ending 180 days after the date of this prospectus, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any ordinary shares or any securities convertible into or exercisable or exchangeable for ordinary shares; or enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our ordinary shares, whether any transaction described above is to be settled by delivery of our ordinary shares or such other securities, in cash or otherwise.

Upon the expiration of the lock-up period, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above. For a further description of these lock-up agreements, please see "Underwriting."

## Rule 144

### *Affiliate Resales of Restricted Securities*

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned ordinary shares for at least six months would be entitled to sell in "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 April 30, 2018; or

- the average weekly trading volume in our ordinary shares on the Nasdaq Global Select 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.

Certain of our existing shareholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share. Any such shares purchased by shareholders who are considered to be our affiliates cannot be resold in the public market immediately following this offering as a result of restrictions under securities laws, but will be able to be sold following the expiration of these restrictions, as described above However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering.

***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 CAYMAN ISLANDS TAX CONSIDERATIONS

The following discussion is a summary of the material Cayman Islands tax considerations relating to the purchase, ownership and disposition of our ordinary shares. There is, at present, no direct taxation in the Cayman Islands and interest, dividends and gains payable to the company will be received free of all Cayman Islands taxes. The company has received an undertaking from the Government of the Cayman Islands to the effect that, for a period of twenty years from the date of the undertaking, no law that thereafter is enacted in the Cayman Islands imposing any tax or duty to be levied on profits, income or on gains or appreciation, or any tax in the nature of estate duty or inheritance tax, will apply to any property comprised in or any income arising under the company, or to the shareholders thereof, in respect of any such property or income.

No stamp duty in the Cayman Islands is payable in respect of the issue of any ordinary shares or an instrument of transfer in respect of an ordinary share.

## CERTAIN UNITED KINGDOM TAX CONSIDERATIONS

The following statements are of a general nature and do not purport to be a complete analysis of all potential UK tax consequences of acquiring, holding and disposing of our ordinary shares. They are based on current UK tax law and on the current published practice of Her Majesty's Revenue and Customs ("**HMRC**") (which may not be binding on HMRC), as of the date of this prospectus, all of which are subject to change, possibly with retrospective effect. They are intended to address only certain United Kingdom tax consequences for holders of our ordinary shares who are tax resident in (and only in) the United Kingdom, and in the case of individuals, domiciled in (and only in) the United Kingdom (except where expressly stated otherwise) who are the absolute beneficial owners of our ordinary shares and any dividends paid on them and who hold our ordinary shares as investments (other than in an individual savings account or a self-invested personal pension). They do not address the UK tax consequences which may be relevant to certain classes of holders of our ordinary shares such as traders, brokers, dealers, banks, financial institutions, insurance companies, investment companies, collective investment schemes, tax-exempt organizations, trustees, persons connected with us or a member of our group, persons holding our ordinary shares as part of hedging or conversion transactions, holders of our ordinary shares who have (or are deemed to have) acquired our ordinary shares by virtue of an office or employment, and holders of our ordinary shares who are or have been officers or employees of us or a company forming part of our group. The statements do not apply to any holder of our ordinary shares who either directly or indirectly holds or controls 10% or more of the our share capital (or class thereof), voting power or profits.

The following is intended only as a general guide and is not intended to be, nor should it be considered to be, legal or tax advice to any particular prospective subscriber for, or purchaser of, our ordinary shares. Accordingly, prospective subscribers for, or purchasers of, our ordinary shares who are in any doubt as to their tax position regarding the acquisition, ownership and disposition of our ordinary shares or who are subject to tax in a jurisdiction other than the United Kingdom should consult their own tax advisers.

### The Company

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

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

### Taxation of dividends

#### *Withholding tax*

We will not be required to withhold UK tax at source when paying dividends on our ordinary shares.

#### *Income tax*

An individual holder of our ordinary shares who is resident for tax purposes in the UK may, depending on his or her particular circumstances, be subject to UK tax on dividends received from us. Dividend income is treated as the top slice of the total income chargeable to UK income tax. An individual holder of our ordinary shares who is not resident for tax purposes in the UK should not be chargeable to UK income tax on dividends received from us unless he or she carries on (whether solely or in partnership) any trade, profession or vocation in the UK through a permanent establishment to which our ordinary shares are attributable. There are certain exceptions for trading in the UK through independent agents, such as some brokers and investment managers.

All dividends received by a UK resident individual holder of our ordinary shares from us or from other sources will form part of that holder's total income for income tax purposes and will constitute the top slice of that income. A nil rate of income tax will apply to the first £2,000 of taxable dividend income received by the holder of our ordinary shares in a tax year. Income within the nil rate band will be taken into account in determining whether income in excess of the nil rate band falls within the basic rate, higher rate or additional rate tax bands. Where the dividend income is above the £2,000 dividend allowance, the first £2,000 of the dividend income will be charged at the nil rate and any excess amount will be taxed at 7.5 per cent. to the extent that the excess amount falls within the basic rate tax band, 32.5 per cent. to the extent that the excess amount falls within the higher rate tax band and 38.1 per cent. to the extent that the excess amount falls within the additional rate tax band.

***Corporation tax***

Corporate holders of our ordinary shares which are resident for tax purposes in the UK should not be subject to UK corporation tax on any dividend received from us so long as the dividends qualify for exemption (as is likely) and certain conditions are met (including anti-avoidance conditions). Corporate holders of our ordinary shares which are not resident in the United Kingdom will not generally be subject to UK corporation tax on dividends unless they are carrying on a trade, profession or vocation in the United Kingdom through a permanent establishment in connection with which such shares are attributable.

A holder of our ordinary shares who is resident outside the United Kingdom may be subject to non-UK taxation on dividend income under local law.

**Taxation of capital gains**

***UK resident holders of our ordinary shares***

A disposal or deemed disposal of our ordinary shares by an individual or corporate holder of such shares who is tax resident in the United Kingdom may, depending on that holder's circumstances and subject to any available exemptions or reliefs, give rise to a chargeable gain or allowable loss for the purposes of UK taxation of chargeable gains.

Any chargeable gain (or allowable loss) will generally be calculated by reference to the consideration received for the disposal of our ordinary shares less the allowable cost to the holder of acquiring such shares.

The applicable tax rates for individual holders of our ordinary shares realizing a gain on the disposal of such shares is, broadly, 10% for basic rate taxpayers and 20% for higher and additional rate taxpayers. The applicable tax rates for corporate holders of our ordinary shares realizing a gain on the disposal of such shares is currently 19%.

***Non-UK holders of our ordinary shares***

Holders of our ordinary shares who are not resident in the United Kingdom and, in the case of an individual holder of our ordinary shares, not temporarily non-resident, should not be liable for UK tax on capital gains realized on a sale or other disposal of our ordinary shares unless such shares are attributable to a trade, profession or vocation carried on in the United Kingdom through a branch or agency or, in the case of a corporate holder of our ordinary shares, through a permanent establishment. Holders of our ordinary shares who are not resident in the United Kingdom may be subject to non-UK taxation on any gain under local law.

Generally, an individual holder of our ordinary shares who has ceased to be resident in the United Kingdom for tax purposes for a period of five years or less and who disposes of our ordinary shares during that period may be liable on their return to the United Kingdom to UK taxation on any capital gain realized (subject to any available exemption or relief).

**UK stamp duty (“Stamp Duty”) and UK stamp duty reserve tax (“SDRT”)**

The statements below are intended as a general guide to the current position relating to Stamp Duty and SDRT and apply to any holders of our ordinary shares irrespective of their place of tax residence.

No UK Stamp Duty or SDRT, will be payable on the issue of ordinary shares, subject to the comments below.

Stamp Duty will in principle be payable on any instrument of transfer of ordinary shares that is executed in the United Kingdom or that relates to any property situated, or to any matter or thing done or to be done, in the United Kingdom. An exemption from Stamp Duty is available on an instrument transferring ordinary shares where the amount or value of the consideration is £1,000 or less and it is certified on the instrument that the transaction effected by the instrument does not form part of a larger transaction or series of transactions in respect of which the aggregate amount or value of the consideration exceeds £1,000. Holders of ordinary shares should be aware that, even where an instrument of transfer is in principle subject to Stamp Duty, Stamp Duty is not required to be paid unless it is necessary to rely on the instrument for legal purposes, for example to register a change of ownership or in litigation in a UK court.

Provided that ordinary shares are not registered in any register maintained in the United Kingdom by or on behalf of us and are not paired with any shares issued by a UK incorporated company, any agreement to transfer ordinary shares will not be subject to SDRT. The ordinary shares are not paired with any shares issued by a UK incorporated company and we currently do not intend that any register of ordinary shares will be maintained in the United Kingdom.

If ordinary shares were to be registered in a register maintained in the United Kingdom by or on behalf of us or paired with any shares issued by a UK incorporated company then, subject to the comments below, where ordinary shares are transferred or issued to, or to a nominee or agent for, a person whose business is or includes the provision of clearance services or issuing depositary receipts (but not including CREST), SDRT may be payable at a rate of 1.5% of the amount or value of the consideration payable for (or, in certain circumstances, the value of) the ordinary shares. This liability for SDRT will be payable by the clearance service or depositary receipt operator or its nominee, as the case may be, but in practice participants in the clearance service or depositary receipt scheme will generally be required to reimburse them for such cost. It is understood that H.M. Revenue and Customs regards the facilities of DTC as a clearance service for these purposes.

Following litigation, H.M. Revenue and Customs has confirmed that it will no longer seek to apply the above 1.5% SDRT charge (or a corresponding Stamp Duty charge) on the issue of shares into a clearance service or depositary receipt system established in a European Member State on the basis that the charge is not compatible with EU law. However, their view is that the 1.5% charge will still apply to the transfer of shares into such a clearance service or depositary receipts system where the transfer is not an integral part of the issue of share capital. There is an exception from the 1.5% charge on the transfer to, or to a nominee or agent for, a clearance service where the clearance service has made and maintained an election under section 97A(1) of the UK Finance Act 1986 which has been approved by HMRC. We are not aware of any section 97A election having been made by DTC. Accordingly, holders of ordinary shares should consult their own independent professional advisers before incurring or reimbursing the costs of such a 1.5% SDRT charge.

## MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES

The following discussion describes the material U.S. federal income tax consequences to U.S. Holders (as defined below) under present law of an investment in our ordinary shares. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire the ordinary shares. The effects of any applicable state or local laws, other U.S. federal tax laws such as estate and gift tax laws, the alternative minimum tax or the Medicare contribution tax on net investment income, are not discussed. This summary applies only to investors who acquire the ordinary shares in exchange for cash, hold the ordinary shares as capital assets (generally, property held for investment) and who have the U.S. dollar as their functional currency. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, U.S. Treasury regulations promulgated thereunder, judicial decisions, published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or the IRS, all as in effect as of the date of this prospectus. All of the foregoing authorities are subject to change, which change could apply retroactively and could alter the tax consequences described below.

The following discussion does not address all U.S. federal income tax consequences relevant to a holder's particular circumstances or to holders subject to particular rules, including:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons whose functional currency is not the U.S. dollar;
- persons holding ordinary shares as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers or traders in securities, commodities or currencies;
- S corporations or entities or arrangements treated as partnerships for U.S. federal income tax purposes;
- tax-exempt organizations or governmental organizations;
- individual retirement accounts or other tax deferred accounts;
- persons who acquired the ordinary shares pursuant to the exercise of any employee share option or otherwise as compensation;
- persons that own or are deemed to own 10% or more of our stock by vote or value;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to the ordinary shares being taken into account in an applicable financial statement;
- persons that hold ordinary shares through a permanent establishment or fixed base outside the United States; and
- persons deemed to sell ordinary shares under the constructive sale provisions of the Code.

**U.S. HOLDERS ARE URGED TO CONSULT THEIR TAX ADVISORS REGARDING THE APPLICATION OF THE U.S. FEDERAL TAX RULES TO THEIR PARTICULAR CIRCUMSTANCES AS WELL AS THE U.S. STATE, LOCAL AND NON-U.S. TAX CONSEQUENCES TO THEM OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF ORDINARY SHARES.**

For purposes of this discussion, a "U.S. Holder" is a beneficial owner of ordinary shares that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;

- 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.

Certain of our existing shareholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $40.0 million of our ordinary shares in this offering at the initial public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to any of these potential purchasers, and any of these potential purchasers could determine to purchase more, fewer or no shares in this offering. The underwriters will receive the same underwriting discount and commissions on these shares as they will on any other shares sold to the public in this offering.

### 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 $50,000 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 | $ | $ | $ |
| MeiraGTx Holdings plc | | | |

The expenses of the offering, not including the underwriting discount, are estimated at $2,750,000 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 750,000 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 substantially all of 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 Select Market Listing

Our ordinary shares have been approved for listing on the Nasdaq Global Select 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 Select 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 our ordinary shares and certain other matters of Cayman Islands law will be passed upon for us by Walkers, 190 Elgin Avenue, George Town, Grand Cayman KY1-9001, Cayman Islands. Certain other matters will be passed upon for us by Latham & Watkins LLP. Certain legal matters in connection with this offering will be passed upon for the underwriters by Cooley LLP.

## EXPERTS

The consolidated financial statements of MeiraGTx Limited and Subsidiaries at December 31, 2017 and 2016, and for each of the two years in the period ended December 31, 2017, appearing in this Prospectus and Registration Statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements) appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

## ENFORCEMENT OF CIVIL LIABILITIES

We are incorporated under the laws of the Cayman Islands. We have been advised that there is some doubt as to the enforceability in the Cayman Islands, in original actions or in actions for enforcement of judgments of U.S. courts, of civil liabilities based solely on the federal securities laws of the United States. In addition, awards for punitive damages in actions brought in the United States or elsewhere may be unenforceable in the Cayman Islands. An award for monetary damages under the U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered and is intended to punish the defendant. The enforceability of any judgment in the Cayman Islands will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and the Cayman Islands do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

We have appointed MeiraGTx, LLC as our agent to receive service of process with respect to any action brought against us in the United States District Court for the Southern District of New York under the federal securities laws of the United States or of any state in the United States or any action brought against us in the Supreme Court of the State of New York in the County of New York under the securities laws of the State of New York.

We have been advised by our Cayman Islands legal counsel that the courts of the Cayman Islands are unlikely (i) to recognize or enforce against us judgments of courts of the United States predicated upon the civil liability provisions of the federal securities laws of the United States or any state; and (ii) in original actions brought in the Cayman Islands, to impose liabilities against us predicated upon the civil liability provisions of the federal securities laws of the United States or any state, so far as the liabilities imposed by those provisions are penal in nature. In those circumstances, although there is no statutory enforcement in the Cayman Islands of judgments obtained in the United States, the courts of the Cayman Islands will recognize and enforce a foreign money judgment of a foreign court of competent jurisdiction without retrial on the merits based on the principle that a judgment of a competent foreign court imposes upon the judgment debtor an obligation to pay the sum for which judgment has been given provided certain conditions are met. For a foreign judgment to be enforced in the Cayman Islands, such judgment must be final and conclusive and for a liquidated sum, and must not be in respect of taxes or a fine or penalty, inconsistent with a Cayman Islands judgment in respect of the same matter, impeachable on the grounds of fraud or obtained in a manner, and or be of a kind the enforcement of which is, contrary to natural justice or the public policy of the Cayman Islands (awards of punitive or multiple damages may well be held to be contrary to public policy). A Cayman Islands Court may stay enforcement proceedings if concurrent proceedings are being brought elsewhere.

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to the ordinary shares offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the ordinary shares offered hereby, we refer you to the registration statement and the exhibits and schedules filed thereto. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. Upon completion of this offering, we will be required to file periodic reports, proxy statements, and other information with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934. You may read and copy this information at the Public Reference Room of the Securities and Exchange Commission, 100 F Street, N.E., Room 1580, Washington, District of Columbia. 20549. You may obtain information on the operation of the public reference rooms by calling the Securities and Exchange Commission at 1-800-SEC-0330. The Securities and Exchange Commission also maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the Securities and Exchange Commission. The address of that site is *www.sec.gov*.

**INDEX TO CONSOLIDATED FINANCIAL STATEMENTS**
**MEIRAGTX LIMITED AND SUBSIDIARIES**
**FOR THE YEARS ENDED DECEMBER 31, 2016 AND 2017**
**AND FOR THE THREE MONTHS ENDED MARCH 31, 2017 AND 2018**

## Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of MeiraGTx Limited and Subsidiaries

**Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of MeiraGTx Limited and Subsidiaries (the Company) as of December 31, 2017 and 2016, the related consolidated statements of operations and comprehensive loss, convertible preferred C shares, shareholders' deficit and cash flows for each of the two years in the period ended December 31, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

**The Company's Ability to Continue as a Going Concern**

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations, is subject to significant uncertainty with respect to its product development and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

**Basis for Opinion**

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2016.

Stamford, Connecticut
March 29, 2018, except for Note 6, as to which the date is May 11, 2018

**MEIRAGTX LIMITED AND SUBSIDIARIES**
**CONSOLIDATED BALANCE SHEETS**

| | December 31, 2016 | December 31, 2017 | March 31, 2018 (unaudited) | Pro Forma March 31, 2018 (unaudited) |
|---|---|---|---|---|
| ASSETS | | | | |
| CURRENT ASSETS: | | | | |
| Cash and cash equivalents | $ 17,476,641 | $ 8,548,638 | $ 32,356,851 | $ 32,356,851 |
| Prepaid expenses | 1,212,183 | 1,961,243 | 2,816,413 | 2,816,413 |
| Other current assets | 400,956 | 965,233 | 841,172 | 841,172 |
| Total Current Assets | 19,089,780 | 11,475,114 | 36,014,436 | 36,014,436 |
| Property and equipment, net | 3,016,525 | 14,255,729 | 14,643,091 | 14,643,091 |
| Restricted cash | 444,844 | 123,376 | 123,376 | 123,376 |
| TOTAL ASSETS | $ 22,551,149 | $ 25,854,219 | $ 50,780,903 | $ 50,780,903 |
| LIABILITIES, CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' DEFICIT | | | | |
| CURRENT LIABILITIES: | | | | |
| Accounts payable | $ 1,474,213 | $ 7,055,380 | $ 5,184,508 | $ 5,184,508 |
| Accrued expenses | 4,018,103 | 9,332,944 | 6,657,257 | 6,657,257 |
| Note payable | — | 1,442,009 | — | — |
| Warrant liability | — | 2,679,633 | 2,010,225 | — |
| Capitalized lease obligation—current portion | 6,015 | 30,850 | 28,715 | 28,715 |
| Due to Kadmon | 543,038 | 861,030 | 6,493 | 6,493 |
| Total Current Liabilities | 6,041,369 | 21,401,846 | 13,887,198 | 11,876,973 |
| Capitalized lease obligation | 5,458 | 34,298 | 28,655 | 28,655 |
| Deferred rent | 588,491 | 266,290 | 241,488 | 241,488 |
| Other liabilities | 221,254 | 178,419 | 187,848 | 187,848 |
| TOTAL LIABILITIES | 6,856,572 | 21,880,853 | 14,345,189 | 12,334,964 |
| COMMITMENTS | | | | |
| CONVERTIBLE PREFERRED C SHARES | | | | |
| Convertible Preferred C Shares 6,111,526, 19,428,037, 36,330,692 and 0 issued and outstanding at December 31, 2016, 2017, March 31, 2018 (unaudited), and pro forma March 31, 2018 (unaudited), respectively (liquidation preference of $33,002,240, $52,455,700, $98,092,869 and 0 at December 31, 2016 and 2017, March 31, 2018 (unaudited) and pro forma March 31, 2018 (unaudited) respectively) | 32,833,660 | 51,338,631 | 97,351,080 | — |
| SHAREHOLDERS' DEFICIT: | | | | |
| Ordinary Shares, $0.00001 nominal value | 342 | 342 | 364 | 763 |
| 34,224,578 issued and 32,712,995 issued and outstanding at December 31, 2016 | | | | |
| 34,254,578 issued and 33,821,221 issued and outstanding at December 31, 2017 | | | | |
| 36,389,760 issued and 36,235,113 issued and outstanding at March 31, 2018 (unaudited) | | | | |
| 76,320,452 issued and outstanding at pro forma March 31, 2018 (unaudited) | | | | |
| Capital in excess of nominal value | 17,900,995 | 20,080,713 | 23,691,708 | 123,228,597 |
| Accumulated other comprehensive loss | (661,112) | (2,022,477) | (2,780,242) | (2,780,242) |
| Accumulated deficit | (34,379,308) | (65,423,843) | (81,827,196) | (82,003,179) |
| Total Shareholders' Deficit | (17,139,083) | (47,365,265) | (60,915,366) | 38,445,939 |
| TOTAL LIABILITIES, CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' DEFICIT | $ 22,551,149 | $ 25,854,219 | $ 50,780,903 | $ 50,780,903 |

See Notes to Consolidated Financial Statements

## MEIRAGTX LIMITED AND SUBSIDIARIES
## CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

| | For the Years Ended December 31, | | For the Three-Month Periods Ended March 31, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 (unaudited) | 2018 (unaudited) |
| Operating expenses: | | | | |
| General and administrative | 6,026,529 | 9,325,017 | 2,148,540 | 11,122,016 |
| Research and development | 14,037,918 | 22,359,712 | 4,823,357 | 6,927,322 |
| Total operating expenses | 20,064,447 | 31,684,729 | 6,971,897 | 18,049,338 |
| Loss from operations | (20,064,447) | (31,684,729) | (6,971,897) | (18,049,338) |
| Other non-operating income (expense) | | | | |
| Foreign currency gain | 265,543 | 1,676,117 | 149,249 | 978,624 |
| Convertible note inducement expense | — | (553,500) | — | — |
| Change in fair value of warrant liability | — | (465,633) | — | 669,408 |
| Interest income | 32,068 | 26,073 | 10,389 | 25,308 |
| Interest expense | (25,440) | (42,863) | (8,126) | (27,355) |
| Net loss | (19,792,276) | (31,044,535) | (6,820,385) | (16,403,353) |
| Net loss attributable to the non-controlling interest in subsidiary | 305,883 | — | — | — |
| Net loss attributable to MeiraGTx Limited shareholders | (19,486,393) | (31,044,535) | (6,820,385) | (16,403,353) |
| Other comprehensive loss | (671,391) | (1,361,365) | (130,895) | (757,765) |
| Comprehensive loss | (20,157,784) | (32,405,900) | (6,951,280) | (17,161,118) |
| Less: comprehensive loss attributable to noncontrolling interest | 8,520 | — | — | — |
| Comprehensive loss attributable to MeiraGTx Limited shareholders | $ (20,149,264) | $ (32,405,900) | $ (6,951,280) | $ (17,161,118) |
| Net loss attributable to MeiraGTx Limited shareholders | $ (19,486,393) | $ (31,044,535) | $ (6,820,385) | $ (16,403,353) |
| Accretion on convertible preferred C shares | (85,425) | (806,963) | (22,761) | (664,718) |
| Adjusted net loss attributable to MeiraGTx Limited ordinary shareholders | $ (19,571,818) | $ (31,851,498) | $ (6,843,146) | $ (17,068,071) |
| Basic and diluted net loss per ordinary share attributable to ordinary shareholders | $ (0.63) | $ (0.96) | $ (0.21) | $ (0.49) |
| Weighted-average number of ordinary shares outstanding | 31,098,591 | 33,269,157 | 32,851,408 | 34,647,368 |
| Pro forma adjusted net loss attributable to MeiraGTx Limited ordinary shareholders (unaudited) | | $ (30,754,885) | | $ (17,072,761) |
| Pro forma basic and diluted net loss per ordinary share attributable to ordinary shareholders (unaudited) | | $ (0.42) | | $ (0.23) |
| Pro forma weighted-average number of ordinary shares outstanding—basic and diluted (unaudited) | | 73,289,247 | | 74,667,458 |

See Notes to Consolidated Financial Statements

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**MEIRAGTX LIMITED AND SUBSIDIARIES**
**CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' DEFICIT**
**AS OF MARCH 31, 2018**

| | Convertible Preferred C Shares | | Shareholders' Deficit | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Convertible Preferred C Shares | Amount | A Ordinary Shares | B Ordinary Shares | Amount | Capital in Excess of Nominal Value | Accumulated Other Comprehensive Income (Loss) | Non-Controlling Interest in Subsidiary | Accumulated Deficit | Shareholders' Deficit |
| Balance at December 31, 2015 | 1,944,440 | $ 10,416,205 | 29,851,230 | 10,000 | $ 299 | $ 15,594,166 | $ 1,759 | $ (789,698) | $(14,892,915) | $ (86,389) |
| Issuance of A ordinary shares in connection with the Acquisition of BRI-Alzan, Inc. | — | — | 300,000 | — | 3 | 597,297 | — | — | — | 597,300 |
| Issuance of A ordinary shares in connection with acquisition of non-controlling interest of MeiraGTx UK II Limited | — | — | 4,017,048 | — | 40 | (1,104,141) | — | 1,104,101 | — | — |
| Issuance of convertible preferred C shares in connection with a payable | 230,000 | 1,242,000 | — | — | — | — | — | — | — | — |
| Issuance of A ordinary shares in connection with a consulting agreement | — | — | 46,300 | — | — | 92,137 | — | — | — | 92,137 |
| Conversion of B ordinary shares into A ordinary shares | — | — | 10,000 | (10,000) | — | — | — | — | — | — |
| Issuance of convertible preferred C shares in connection with a research agreement | 59,259 | 319,999 | — | — | — | — | — | — | — | — |
| Issuance of convertible preferred C shares, net of issuance costs | 3,877,827 | 20,770,031 | — | — | — | — | — | — | — | — |
| Accretion of issuance costs on convertible preferred C shares | — | 85,425 | — | — | — | (85,425) | — | — | — | (85,425) |
| Share-based compensation | — | — | — | — | — | 2,806,961 | — | — | — | 2,806,961 |
| Foreign currency translation | — | — | — | — | — | — | (662,871) | (8,520) | — | (671,391) |
| Net loss for the year ended December 31, 2016 | — | — | — | — | — | — | — | (305,883) | (19,486,393) | (19,792,276) |
| Balance at December 31, 2016 | 6,111,526 | $ 32,833,660 | 34,224,578 | — | $ 342 | $ 17,900,995 | $ (661,112) | $ — | $(34,379,308) | $(17,139,083) |
| Exercised stock options | — | — | 5,000 | — | — | 9,950 | — | — | — | 9,950 |
| Issuance of A ordinary shares in connection with a license agreement | — | — | 25,000 | — | — | 17,000 | — | — | — | 17,000 |
| Extinguishment of convertible preferred C shares, net of unaccreted issuance costs | (6,149,326) | (33,115,157) | — | — | — | 33,115,157 | — | — | — | 33,115,157 |
| Issuance of convertible preferred C shares in connection with extinguishment | 12,298,652 | 33,206,360 | — | — | — | (33,206,360) | — | — | — | (33,206,360) |
| Conversion of note payable into convertible preferred C shares | 925,926 | 2,500,000 | — | — | — | — | — | — | — | — |
| Issuance of convertible preferred C shares, net of warrants and issuance costs | 6,241,259 | 15,198,008 | — | — | — | — | — | — | — | — |
| Accretion of issuance costs on convertible preferred C shares | — | 100,760 | — | — | — | (100,760) | — | — | — | (100,760) |
| Accretion of warrants issued in connection with convertible preferred C shares | — | 615,000 | — | — | — | (615,000) | — | — | — | (615,000) |
| Share-based compensation | — | — | — | — | — | 2,959,731 | — | — | — | 2,959,731 |
| Foreign currency translation | — | — | — | — | — | — | (1,361,365) | — | — | (1,361,365) |
| Net loss for the year ended December 31, 2017 | — | — | — | — | — | — | — | — | (31,044,535) | (31,044,535) |
| Balance at December 31, 2017 | 19,428,037 | 51,338,631 | 34,254,578 | — | $ 342 | $ 20,080,713 | $ (2,022,477) | $ — | $(65,423,843) | $(47,365,265) |
| Issuance of convertible preferred C shares in connection with payables | 502,270 | 1,356,129 | — | — | — | — | — | — | — | — |
| Issuance of preferred C shares in connection with a license agreement | 51,852 | 140,000 | — | — | — | — | — | — | — | — |
| Issuance of convertible preferred C shares, net of issuance costs | 16,348,533 | 43,851,602 | — | — | — | — | — | — | — | — |
| Accretion of issuance costs on convertible preferred C shares | — | 94,445 | — | — | — | (94,445) | — | — | — | (94,445) |
| Accretion of warrants issued in connection with convertible preferred C shares | — | 570,273 | — | — | — | (570,273) | — | — | — | (570,273) |
| Share-based compensation | — | — | 2,135,182 | — | 22 | 4,275,713 | — | — | — | 4,275,735 |
| Foreign currency translation | — | — | — | — | — | — | (757,765) | — | — | (757,765) |
| Net loss for the three-month period ended March 31, 2018 | — | — | — | — | — | — | — | — | (16,403,353) | (16,403,353) |
| Balance at March 31, 2018 (unaudited) | 36,330,692 | $ 97,351,080 | 36,389,760 | — | $ 364 | $ 23,691,708 | $ (2,780,242) | $ — | $(81,827,196) | $(60,915,366) |

See Notes to Consolidated Financial Statements

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# MEIRAGTX LIMITED AND SUBSIDIARIES
# CONSOLIDATED STATEMENTS OF CASH FLOWS

| | For the Year Ended December 31, 2016 | For the Year Ended December 31, 2017 | For the Three-Month Period Ended March 31, 2017 (unaudited) | For the Three-Month Period Ended March 31, 2018 (unaudited) |
|---|---|---|---|---|
| Cash flows from operating activities: | | | | |
| Net loss | $ (19,792,276) | $ (31,044,535) | $ (6,820,385) | $ (16,403,353) |
| 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 | 844,237 | 4,275,735 |
| Foreign currency loss (gain) | (261,817) | (1,676,117) | (149,249) | (978,624) |
| Depreciation | 243,081 | 679,177 | 179,878 | 458,836 |
| Amortization of interest on asset retirement obligation | 17,248 | 19,313 | 4,507 | 3,678 |
| Change in fair value of warrant liability | — | 465,633 | — | (669,408) |
| Convertible note inducement expense | — | 553,500 | — | — |
| Acquired research and development expense | 597,300 | — | — | — |
| Issuance of note payable in connection with lease termination | — | 1,442,009 | — | — |
| Preferred C shares issued in connection with a license agreement | — | — | — | 140,000 |
| (Increase) decrease in operating assets: | | | | |
| Prepaid expenses and other current assets | (960,993) | (669,756) | (122,914) | (821,062) |
| Other current assets | (302,901) | (493,424) | (338,126) | 153,773 |
| Increase (decrease) in operating liabilities: | | | | |
| Accounts payable | 453,130 | 4,728,491 | 842,876 | 171,045 |
| Accrued expenses | 1,333,796 | 4,969,619 | (1,147,336) | (2,846,292) |
| Due to Kadmon | 800,223 | 317,992 | (128,974) | (854,537) |
| Deferred rent | 255,160 | (324,019) | 389,928 | (25,760) |
| Other liabilities | — | — | 50,220 | — |
| **Net cash used in operating activities** | (14,367,952) | (18,055,386) | (6,395,338) | (17,395,969) |
| Cash flows from investing activities: | | | | |
| Purchase of property and equipment | (2,593,584) | (10,535,717) | (1,737,520) | (1,210,452) |
| **Net cash used in investing activities** | (2,593,584) | (10,535,717) | (1,737,520) | (1,210,452) |
| Cash flows from financing activities: | | | | |
| Payments on capitaized lease obligation | (5,480) | (24,388) | (1,452) | (7,779) |
| Proceeds from the issuance of note payable | — | 2,500,000 | — | — |
| Proceeds from the issuance of convertible preferred C shares, net of issuance costs | 20,762,682 | 16,854,653 | 197,995 | 43,851,602 |
| Proceeds from exercised stock options | — | 9,950 | — | — |
| Payment of note payable | — | — | — | (1,442,009) |
| **Net cash provided by financing activities** | 20,757,202 | 19,340,215 | 196,543 | 42,401,814 |
| Net increase (decrease) in cash, cash equivalents and restricted cash | 3,795,666 | (9,250,888) | (7,936,315) | 23,795,393 |
| Effect of exchange rate changes on cash | (421,240) | 1,417 | (11,109) | 12,820 |
| Cash, cash equivalents and restricted cash at beginning of period | 14,547,059 | 17,921,485 | 17,921,485 | 8,672,014 |
| Cash, cash equivalents and restricted cash at end of period | $ 17,921,485 | $ 8,672,014 | $ 9,974,061 | $ 32,480,227 |
| **Supplemental disclosure of non-cash transactions:** | | | | |
| Fixed asset acquisition included in accounts payable and accrued expenses | $ 301,655 | $ 415,650 | $ 766,107 | $ (811,095) |
| Conversion of note payable into convertible preferred C shares | $ — | $ 2,500,000 | $ — | $ — |
| Issuance of convertible preferred C shares in connection with payables | $ — | $ — | $ — | $ 1,356,129 |
| Capitalized lease obligation for equipment purchase | $ 17,817 | $ 78,063 | $ — | $ — |
| Issuance of convertible preferred C shares in settlement of due to Kadmon | $ 1,242,000 | $ — | $ — | $ — |
| Issuance of A ordinary shares for acquisition of BRI-Alzan | $ 597,300 | $ — | $ — | $ — |
| Issuance of convertible preferred C shares in connection with a research agreement | $ 320,000 | $ — | $ — | $ — |
| Asset retirement obligation in connection with a lease | $ 205,659 | $ (75,011) | $ — | $ — |
| **Supplemental disclosure of cash flow information:** | | | | |
| Cash paid for interest | $ — | $ 20,894 | $ 257 | $ 31,531 |

See Notes to Consolidated Financial Statements

**MEIRAGTX LIMITED AND SUBSIDIARIES**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**1. Principal Business Activity:**

***The Company***

MeiraGTx Limited (the "Company" or "Meira Limited"), a limited company under the laws of England and Wales formed on March 20, 2015, is a clinical-stage biotech company developing novel gene therapy treatments for a wide range of inherited and acquired disorders for which there are no effective treatments available. The Company is focused on developing therapies for ocular diseases, including rare inherited blindness as well as Xerostomia following radiation treatment for head and neck cancers and neurodegenerative diseases such as 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 15).

On April 27, 2015, the Company entered into a worldwide collaborative development and license agreement ("CDLA") with Athena Vision Limited ("Athena") to develop and commercialize pre-clinical gene therapies for certain ocular indications. Concurrent with the execution of the CDLA, the Company and Athena entered into a shareholders' agreement in which the Company issued 2,760,000 A ordinary shares ("Ordinary Shares") and 250 B ordinary shares, which were converted into Ordinary Shares, to the shareholders of Athena in exchange for a 60% equity interest in Athena.

On April 8, 2016, the Company issued 4,017,048 Ordinary Shares to the shareholders of Athena in exchange for the remaining 40% equity interest in Athena and changed the name of Athena to MeiraGTx UK II Limited ("MeiraGTx UK II").

***Basis of Presentation***

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

On April 27, 2015, the Company acquired as 60% interest in MeiraGTx UK II. As such, a non-controlling interest was recorded on the date of acquisition through April 8, 2016, when the Company acquired the remaining 40% interest in MeiraGTx UK II.

***Liquidity***

The consolidated financial statements of the Company have been prepared on a going-concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. Accordingly, the financial statements do not include any adjustments that might be necessary should the Company be unable to continue in existence. The Company has not generated any revenues and has not yet achieved profitable operations. There is no assurance that profitable operations, if ever achieved, could be sustained on a continuing basis. In addition, development activities, clinical and preclinical testing, and commercialization of the Company's product candidates will require significant additional financing. The Company's accumulated deficit at December 31, 2017 and March 31, 2018 totaled $65,423,843 and $81,827,196, respectively, and management expects to incur substantial and increasing losses in future periods. The success of the Company is subject to certain risks and uncertainties, including among others, uncertainty of product development; competition in the Company's field of use; uncertainty of capital availability; uncertainty in the Company's ability to enter into agreements with collaborative partners; dependence on third parties; and dependence on key personnel. The Company has not generated positive cash flows from operations, and there are no assurances that the Company will be successful in obtaining an adequate level of financing for the development and commercialization of its product candidates. These factors raise substantial doubt about the Company's ability to continue as a going concern. The Company does not have adequate cash on hand to cover its anticipated expenses past the next 12 months. If the Company fails to raise a significant amount of capital or enter into a strategic transaction, it may need to significantly curtail operations, cease operations or seek federal bankruptcy protection in the near future. These conditions raise substantial doubt about its ability to continue as a going concern.

As of December 31, 2017, the Company had cash and cash equivalents in the amount of $8,548,638, which consisted of depository accounts. From January 1, 2018 through March 29, 2018, the Company issued 16,943,396 convertible preferred C shares ("Preferred Shares") for gross proceeds of $45,747,173. The Company estimates that its cash and cash equivalents on hand at December 31, 2017 and the proceeds from the issuance of Preferred Shares from January 1, 2018 through March 29, 2018 will cover its expenses into the fourth quarter of 2018.

As of March 31, 2018, the Company had cash and cash equivalents in the amount of $32,356,851, which consisted of depository accounts. From April 1, 2018 through April 30, 2018, the company issued 4,597,637 Preferred Shares for gross proceeds of $12,413,619. The Company estimates that its cash and cash equivalents on hand at March 31, 2018 and the proceeds from the issuance of Preferred Shares from April 1, 2018 through April 30, 2018 will cover its expenses into the first quarter of 2019.

In order to provide the Company with the cash resources necessary to fund operations, the Company will continue its efforts to raise additional capital through either a private or public equity placement or strategic transaction in the near future.

If the Company is unable to raise additional funds, it will need to do one or more of the following:

- license third parties to develop and commercialize products or technologies that it would otherwise seek to develop and commercialize itself;
- seek strategic alliances or business combinations;
- attempt to sell the Company;
- cease operations; or
- declare bankruptcy.

***Risks and Uncertainties***

The Company operates in an industry that is subject to intense competition, government regulation and rapid technological change. The Company's operations are subject to significant risk and uncertainties including financial, operational, technological, regulatory and other risks, including the potential risk of business failure.

**MEIRAGTX LIMITED AND SUBSIDIARIES**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

The Company's limited capital resources and operations to date have been funded primarily with the proceeds from private equity.

***Reverse Stock Split***

The Company's shareholders approved a 10:1 stock split, effective February 2, 2016. All share information presented in these financial statements and accompanying footnotes have been retroactively adjusted to reflect the increased number of shares resulting from this action.

**2. Summary of Significant Accounting Policies:**

***Consolidation***

The accompanying condensed consolidated financial statements include the accounts of Meira Limited and its wholly owned subsidiaries:

MeiraGTx, LLC, a Delaware corporation, ("Meira LLC");

BRI-Alzan, Inc., a Delaware corporation ("BRI-Alzan");

MeiraGTx B.V., a Netherlands corporation ("Meira BV");

MeiraGTx UK II Limited, ("Meira UK II"), a limited company under the laws of England and Wales;

MeiraGTx UK Limited ("Meira UK"), a limited company under the laws of England and Wales.

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

***Unaudited Interim Financial Statements***

The accompanying interim consolidated balance sheet as of March 31, 2018, the consolidated statements of operations and comprehensive loss and consolidated statements of cash flows for the three months ended March 31, 2017 and 2018, the statement of convertible preferred C shares and stockholders' deficit for the three months ended March 31, 2018, and the financial data and other information disclosed in these notes related to the three months ended March 31, 2017 and 2018 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the audited annual financial statements, and, in the opinion of management, reflect all adjustments, consisting of normal recurring adjustments, necessary for the fair presentation of the Company's financial position as of March 31, 2018, and the results of its operations and its cash flows for the three month ended March 31, 2017 and 2018. The results as of and for the three months ended March 31, 2018 are not necessarily indicative of the results to be expected for the year ending December 31, 2018, any other interim periods, or any future year or period.

***Unaudited Pro Forma Financial Information***

The accompanying unaudited pro forma consolidated balance sheet as of March 31, 2018 has been prepared to give effect to (1) the automatic conversion of all outstanding shares of convertible preferred C shares into ordinary shares, based on a conversion ratio currently in effect, which is 1:1, (2) the vesting of certain previously unvested restricted shares upon the completion of an initial public offering and (3) the reclassification of the warrant liability into capital in excess of nominal value. The ordinary shares issuable and the proceeds expected to be received in the initial public offering and ordinary shares to be granted on the effectiveness of this registration statement to the CEO and COO are excluded from such pro forma financial information.

**MEIRAGTX LIMITED AND SUBSIDIARIES**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

In the accompanying consolidated statements of operations, the unaudited pro forma adjusted net loss attributable to MeiraGTx Limited ordinary shareholders used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to ordinary shareholders does not include the effects of accretion on convertible preferred C shares or the remeasurement of the warrants to purchase convertible preferred C shares because it assumes that the conversion of convertible preferred C shares into ordinary shares and conversion of convertible preferred C share warrant into ordinary shares occurred on the beginning of the reporting period for the year ended December 31, 2017.

***Unaudited Pro Forma Net Loss per Share***

Pro forma basic and diluted net loss per share attributable to ordinary shareholders has been computed to give effect to the conversion of all outstanding convertible preferred shares into ordinary shares. The unaudited pro forma net loss per share does not include the shares expected to be sold and related proceeds to be received from the initial public offering. The unaudited pro forma net loss per share for the twelve months ended December 31, 2017 was computed using the weighted-average number of shares of ordinary shares outstanding, including the pro forma effect of the conversion of all outstanding shares of convertible preferred shares into ordinary shares, including warrant to purchase convertible preferred C shares, as if such conversion had occurred January 1, 2017.

***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. Subsequent events were reviewed through the date of this filing for the years ended December 31, 2016 and 2017 and for the interim financial statements and disclosures for the three months ended March 31, 2017 and 2018. See Note 18 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.

MEIRAGTX LIMITED AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

***Warrant Liability***

During 2017, the Company issued warrants to purchase Preferred Shares to certain investors. Due to the potential redemption feature of the underlying Preferred Shares, the warrants have been classified as a liability. Liability accounting requires that the fair value of warrants be remeasured each reporting period with changes recorded in the statements of operations and comprehensive loss. These Preferred Shares warrants will remain outstanding until the exercise or expiration of the warrants or the completion of a qualified IPO, at which time the warrant liability will be remeasured to fair value and reclassified to additional paid-in capital.

***Financial Instruments***

The carrying value of prepaid expenses, other current assets, accounts payable, accrued expenses, notes payable and amounts due to an affiliate reported in the consolidated balance sheets equal or approximate fair value due to their short maturities.

***Fair Value Measurements***

Fair value is defined as the price that would be received upon sale of an asset or paid upon transfer of a liability in an orderly transaction between market participants at the measurement date and in the principal or most advantageous market for that asset or liability. The fair value should be calculated based on assumptions that market participants would use in pricing the asset or liability, not on assumptions specific to the entity. In addition, the fair value of liabilities should include consideration of non-performance risk including our own credit risk.

The Company follows ASC Topic 820, *Fair Value Measurements and Disclosures*, or ASC 820, for application to financial assets. In addition to defining fair value, the standard expands the disclosure requirements 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.

**MEIRAGTX LIMITED AND SUBSIDIARIES**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

The table below represents the values of the Company's financial assets and liabilities that are required to be measured at fair value on a recurring basis:

| | | 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 |

| | | Fair Value Measurement Using: | | |
|---|---|---|---|---|
| Description | March 31, 2018 | Significant Observable Inputs (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable (Level 3) |
| Restricted cash | $ 123,376 | $ 123,376 | $ — | $ — |
| Warrants | 2,010,225 | — | — | 2,010,225 |
| Total | $ 2,133,601 | $ 123,376 | $ — | $ 2,010,225 |

The table below represents a rollforward of the assets and liabilities that are required to be measured at fair value on a recurring basis from December 31, 2015 to March 31, 2018:

| | Significant Observable Inputs (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
|---|---|---|---|
| Balance as of December 31, 2015 | $ — | $ — | $ — |
| Restriction of cash | 444,844 | — | — |
| Balance as of December 31, 2016 | 444,844 | — | — |
| Cash released from restriction | (321,468) | — | — |
| Fair value of warrants issued | — | — | 2,214,000 |
| Change in fair value of warrants | — | — | 465,633 |
| Balance as of December 31, 2017 | 123,376 | — | 2,679,633 |
| Change in fair value of warrants | — | — | (669,408) |
| Balance as of March 31, 2018 | $ 123,376 | $ — | $ 2,010,225 |

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.

MEIRAGTX LIMITED AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

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 | March 31, 2018 |
|---|---|---|---|---|
| Risk-free interest rate | 1.38% | 1.53% | 1.72% | 1.86% |
| Expected volatility | 80% | 80% | 80% | 80% |
| Expected dividend yield | 0 | 0 | 0 | 0 |
| Expected life | 18 months | 18 months | 9 months | 5.5 months |

For the unobservable inputs for the warrants, the expected volatility was determined at each measurement date by taking an average of the volatility of other publicly-traded peer biotechnology companies. The expected life was determined at each measurement date based upon the Company's estimate of the time until the Company has a conversion event, as described in Note 11.

The fair value of the Preferred Shares was based upon recent issuances of the Company's Preferred Shares on or about these dates.

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

***Convertible Preferred C Shares***

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

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.

**MEIRAGTX LIMITED AND SUBSIDIARIES**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

***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 any of the periods presented.

***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 14).

MEIRAGTX LIMITED AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

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.

Through March 31, 2018, the Company did not have any significant adjustments to the provisional amounts. The Company will continue to analyze the provisional amounts, which are still subject to change during the measurement period, and the Company anticipates further guidance on accounting interpretations from the FASB and application of the law from the Department of the Treasury.

***Research and Development***

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

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

***Share Based Compensation Expense***

*Options*

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

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

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

The third party estimated the fair value of the equity using a special case of the market approach known as the backsolve method. The backsolve method was used to solve for the implied total equity value based on the Company's recent Series C financing round. Consideration was given to the rights and preferences of each of Company's classes of equity and the expected time to a liquidity event. An option pricing allocation method, or OPM, was selected to allocate the total equity value. The OPM treats ordinary shares and preferred shares as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the Ordinary Shares have value only if the funds available for distribution to stockholders exceeded the value of the Preferred Share liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. These third-party valuations resulted in a valuation of the Company's Ordinary Shares of $1.95, $0.68, $1.45 and $1.55 per share as of December 31, 2016, September 15, 2017, December 31, 2017 and March 31, 2018, respectively.

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

Since Company's Ordinary Shares have not been traded on a public exchange, the Company believes that it does not have sufficient company-specific information available to determine the expected term based on its historical data. As a result, the expected term of share options granted to employees and members of the Company's board of directors is determined using the average of the vesting period and contractual life of the option, an accepted method for the Company's option grants under the SEC's Staff Accounting Bulletin No. 107 and No. 110, *Share-Based Payment.*

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

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

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

*Restricted Shares*

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

***Leases***

The Company recognizes rent expense for operating leases on a straight-line basis over the term of the lease, beginning on the date the Company takes possession of the property. Rent expense includes the base amounts stated in the lease agreement as well as the effect of reduced or free rent and rent escalations. At lease inception, the Company determines the lease term by assuming the exercise of those renewal options that are reasonably assured because of the significant economic penalty that exists for not exercising those options. The exercise of renewal options is at the Company's sole discretion. The expected lease term is one of the factors used to determine whether a lease is classified as operating or capital and is used to calculate the straight-line rent expense. The difference between the cash paid to the landlord and the amount recognized as rent expense on a straight-line basis is included in deferred rent and classified within long-term liabilities. Lease incentives made by landlords to or on behalf of the Company for leasehold improvements are recorded as deferred rent and classified as long-term liabilities.

The Company uses estimates to determine the amount of asset retirement obligation at the end of the lease terms and discounts such asset retirement obligations using an estimated discount rate. Interest on the discounted asset retirement obligation is amortized over the term of the lease using the effective interest method and is recorded as interest expense in the consolidated statements of operations and comprehensive loss.

***Asset Retirement Obligation***

Accounting for Asset Retirement Obligations requires legal obligations associated with the retirement of long-lived assets to be recognized at fair value when incurred and capitalized as part of the related long-lived asset. In the absence of quoted market prices, we estimate the fair value of our asset retirement obligations using Level 3 present value techniques, in which estimates of future cash flows associated with retirement activities are discounted using a credit-adjusted risk-free rate. Asset retirement obligations currently reported as other liabilities on our Consolidated Balance Sheet were measured during a period of historically low interest rates. The impact on measurements of new asset retirement obligations using different rates in the future may be significant.

The Company uses estimates to determine the amount of the asset retirement obligations at the end of the lease term and discounts such asset retirement obligations using an estimated discount rate. Interest on the discounted asset retirement obligation is amortized over the term of the lease using the effective interest method and is recorded as interest expense in the consolidated statements of operations and comprehensive loss.

The change in asset retirement obligations is as follows:

| | For the year ended December 31, | | For the three months ended March 31, |
|---|---|---|---|
| | 2016 | 2017 | 2018 |
| Balance at beginning of year | $ — | $ 221,254 | $ 178,419 |
| Inception of asset retirement obligation | 205,659 | — | — |
| Amortization of interest | 17,248 | 19,313 | 3,678 |
| Change in estimate | — | (75,011) | — |
| Effects of exchange rate | (1,653) | 12,863 | 5,751 |
| Balance at end of year | $ 221,254 | $ 178,419 | $ 187,848 |

***Other Comprehensive Loss***

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources.

***Foreign Currencies***

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

***Segment Information***

Management has concluded it has a single reporting segment for purposes of reporting financial condition and results of operations.

The following table summarizes non-current assets by geographical area:

| | December 31, 2016 | December 31, 2017 | March 31, 2018 |
|---|---|---|---|
| United States | $ 1,081,522 | $ 436,463 | $ 411,254 |
| United Kingdom | 2,379,847 | 13,942,642 | 14,355,213 |
| | $ 3,461,369 | $ 14,379,105 | $ 14,766,467 |

*Accounting Pronouncements Recently Adopted*

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718), Scope of Modification Accounting*. ASU 2017-09 provides guidance on the types of changes to the terms or conditions of share-based payment awards to which an entity would be required to apply modification accounting. ASU 2017-09 is applied prospectively to awards modified on or after the effective date. The Company adopted ASU 2017-09 on January 1, 2018. There were no modifications that had an impact on the Company's consolidated financial statements.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations (Topic 805), Clarifying the Definition of a Business*, or ASU 2017-01, that clarifies the definition of a business to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. ASU 2017-01 requires an entity to evaluate if substantially all of the fair value of the gross assets acquired or disposed of is concentrated in a single identifiable asset or a group of similar identifiable assets; if so, the set of transferred assets and activities is not a business. ASU 2017-01 also requires a business to include at least an input and one substantive process that together significantly contribute to the ability to create output and removes the evaluation of whether a market participant could replace missing elements. ASU 2017-01 should be applied prospectively and is effective for annual periods beginning after December 15, 2017 and interim periods within those annual periods. The adoption of ASU 2017-01 on January 1, 2018 did not have a material effect on its financial position, results of operations or cash flows.

In May 2016, the FASB issued ASU No. 2016-12, *Revenue from Contracts with Customers (Topic 606), Narrow-Scope Improvements and Practical Expedients*, or ASU 2016-12, which amends guidance in the new revenue standard, ASU No. 2014-09 *Revenue from Contracts with Customers (Topic 606)*, or ASU 2014-09, on collectability, noncash consideration, presentation of sales tax and transition. The amendments in ASU 2016-12 are effective for annual reporting periods beginning after December 15, 2017 (i.e., January 1, 2018), including interim periods within those reporting periods, which is the same as for ASU 2014-09, as amended by ASU No. 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, or ASU 2015-14. In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with*

*Customers (Topic 606), Identifying Performance Obligations and Licensing*, or ASU 2016-10, which clarifies the principle for determining whether a good or service is "separately identifiable" from other promises in the contract and, therefore, should be accounted for as a separate performance obligation. In that regard, ASU 2016-10 requires that an entity determine whether its promise is to transfer individual goods or services to the customer, or a combined item (or items) to which the individual goods and services are inputs. In addition, ASU 2016-10 categorizes intellectual property, or IP, into two categories: "functional" and "symbolic." Functional IP has significant standalone functionality. All other IP is considered symbolic IP. Revenue from licenses of functional IP is generally recognized at a point in time, while revenue from licenses of symbolic IP is recognized over time. ASU 2016-10 has the same effective date and transition requirements as ASU 2014-09, as amended by ASU 2015-14. In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606)*, *Principal versus Agent Considerations (Reporting Revenue Gross versus Net)*, or ASU 2016-08, which clarifies the implementation guidance on principal versus agent considerations contained in ASU 2014-09 by specifying that the determination as to whether an entity that is involved in providing a good or a service to a customer is a principal or an agent is based upon whether the entity controls the good or the service before it is transferred to the customer. ASU 2016-08 has the same effective date and transition requirements as ASU 2014-09, as amended by ASU 2015-14. The adoption of ASU 2016-20 on January 1, 2018 did not have a material effect on the Company's financial position, results of operations or cash flows.

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers*, or ASU 2014-09, which provides a single, comprehensive revenue recognition model for all contracts with customers. The core principal of ASU 2014-09 is that an entity should recognize revenue when it transfers control of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. ASU 2014-09 is effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2017 for public companies and December 15, 2018 for non-public companies. The Company is allowed to adopt ASU 2014-09 either (1) retrospectively to each prior reporting period presented using several practical expedients related to completed contracts and required disclosures, or (2) using a modified retrospective approach, with the cumulative effect of initially applying ASU 2014-09 recognized as an adjustment to the opening balance of retained earnings of the annual reporting period that includes the date of initial application, including disclosure of the effect of using this method of adoption on the financial statement line items. Because the Company has no contracts with customers, the adoption of ASU 2014-09 on January 1, 2018 did not have a material effect on the Company's financial position, results of operations or cash flows.

In November 2016, the Financial Accounting Standards Board, or FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230), Restricted Cash* (a consensus of the Emerging Issues Task Force), or ASU 2016-18, which changes the presentation of the cash flow statement to include amounts generally described as restricted cash or restricted cash equivalents, together with cash and cash equivalents, when reconciling the beginning-of-period and end-of-period amounts shown on the statement of cash flows. ASU 2016-18 also requires additional disclosures concerning the nature of the restrictions on cash and cash equivalents and a reconciliation between amounts of cash, cash equivalents and restricted cash on the balance sheet and statement of cash flows for each period presented. ASU 2016-18 was applied retrospectively to all periods presented and is effective for public business entities for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. Prior to adoption, the Company presented changes in restricted cash as an operating activity in the statement of cash flows. Upon adoption of ASU 2016-18 on January 1, 2018, such changes are now reflected in the beginning and ending balances of cash, cash equivalents and restricted cash for all periods presented. Cash flows used in operating activities decreased by $441,049 and increased by $321,468 for the years ended December 31, 2016 and 2017, respectively, and $0 for the three month period ended March 31, 2017.

As of December 31, 2016, the Company adopted Accounting Standards Update, or ASU, 2014-15 *Presentation of Financial Statements – Going Concern (Subtopic 205-40), Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASU 2014-15, which is effective for annual periods ending after December 15, 2016, and interim periods within annual periods beginning after December 15, 2016. ASU 2014-15 codifies, for the first time within GAAP, management's responsibility to evaluate whether there is substantial doubt about the Company's ability to continue as a going concern and to provide related footnote disclosures in connection with preparing financial statements for each annual and interim reporting period. Substantial doubt about the Company's ability to continue as a going concern exists when there are conditions or events, considered in the aggregate, that are known and reasonably knowable at the date that the financial statements are issued, that indicate that the Company will be unable to meet its obligations as they become due within one year after that date. In that case, ASU 2014-15 requires the Company to disclose the nature of those conditions or events when they are present, management's plans to mitigate those conditions or events and whether or not such plans alleviated the substantial doubt. Management's evaluation as of the date of issuance of the consolidated financial statements for the year ended December 31, 2017 and three month period ended March 31, 2018 indicate that the Company will not be able to meet its obligations as they become due within one year of the financial statement issuance date (See Note 1).

As of January 1, 2016, the Company adopted ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting*, or ASU 2016-09, which amends Accounting Standards Codification, or ASC, *Topic 718*, *Compensation – Stock Compensation*, and is effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years for public companies and December 15, 2017 for non-public companies. The Company early adopted ASU 2016-09 during the year ended December 31, 2016. ASU 2016-09 simplifies several aspects of the accounting for share-based payment transactions, including the accounting for forfeitures, income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. The amendments will be applied prospectively. Upon adoption, the Company is accounting for forfeitures as they occur rather than estimate a forfeiture rate. As the Company did not issue any stock options prior to the date of adoption and the Company did not record any forfeitures related to restricted share grants to executives in 2015 as there was no expectation that they would leave the Company prior to the vesting dates, a cumulative-effect adjustment was not necessary. In periods subsequent to adoption, a higher expense is recognized earlier during the respective vesting periods of stock-based awards that are not forfeited. The income tax amendments within ASU 2016-09 will have no impact on its results of operations or cash flows because it is in a net operating loss position with a full valuation allowance.

*Recent Accounting Pronouncements Not Yet Adopted*

In December 2016, the FASB issued ASU No. 2016-20, *Technical Corrections and Improvements to Topic 606, Revenue from Contracts with Customers*, or ASU 2016-20, that allows entities not to disclose variable consideration allocated to performance obligations related to either: (1) sales— or usage -based royalties on licenses of intellectual property or (2) variable consideration allocated entirely to a wholly unsatisfied performance obligation or to a wholly unsatisfied promise to transfer a distinct good or service that forms part of a single performance obligation when certain criteria are met. ASU 2016-20 also requires entities that use any of the new or previously existing optional exemptions to expand their qualitative disclosures. It also makes 12 additional technical corrections and improvements to the new revenue standard, ASU 2014-09. The amendments have the same effective date and transition requirements as ASU 2014-09. The Company does not expect the adoption of ASU 2016-20 to have a material effect on its financial position, results of operations or cash flows.

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In October 2016, the FASB issued ASU 2016-16, Income Taxes (Topic 740): *Intra-Entity Transfers of Assets Other than Inventory*, or ASU 2016-16 which requires that an entity recognize the income tax consequences of an intra-entity transfer of assets other than inventory when the transfer occurs. The guidance must be applied using the modified retrospective basis. The Company does not expect the provisions of ASU 2016-16 to have a material impact on its current financial statements. This update will be effective for the Company at the beginning of fiscal 2019.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, or ASU 2016-02, which requires lessees to recognize the following for all leases (with the exception of short-term leases) at the commencement date: a lease liability, which is a lessee's obligation to make lease payments arising from a lease, measured on a discounted basis; and a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term. The revised guidance must be applied on a modified retrospective transition approach for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The revised guidance is effective for the Company at the beginning of Fiscal 2019. The Company is currently evaluating the impact this ASU will have on its consolidated financial statements.

**3. Asset Acquisition:**

Effective January 1, 2016, the Company and BRI-Alzan, Inc. ("BRI-Alzan"), a Delaware corporation, entered into an Agreement and Plan of Merger ("Agreement") to acquire all of the outstanding shares of BRI-Alzan from the shareholders of BRI-Alzan. Prior to entering into the Agreement, BRI-Alzan was an inactive entity that held a worldwide license agreement, dated May 1, 2013, with Brandeis University ("Brandeis") to develop certain pre-clinical technology for the treatment of ALS, but had not yet begun any development activities. In connection with the Agreement, the Company issued 300,000 Ordinary Shares and is required to make certain development milestone payments and royalty payments on the net sales of a product containing the technology in the event that the Company is able to achieve those milestones and develop a marketable product (see Note 15).

The Company determined this transaction represented an asset acquisition as no processes were acquired as defined by ASC 805. The asset acquisition of in process research and development was recorded at a fair value of $597,300 as of January 1, 2016. The acquired in process research and development was immediately charged to research and development expense in the statement of operations and comprehensive loss as of the acquisition date since the Company determined that there was no additional alternative use of these assets. Additionally, under ASC 805, the Company determined that as of the acquisition date and as of December 31, 2016, December 31, 2017 and March 31, 2018, the contingent milestone payments in the aggregate amount of $4,500,000, and royalty payments have not been resolved and therefore have not been recorded as liability.

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**4. Prepaid Expenses:**

Prepaid expenses for the periods presented consist of the following:

| | December 31, 2016 | December 31, 2017 | March 31, 2018 |
|---|---|---|---|
| Research and Development | $ 418,483 | $ 624,348 | $ 630,196 |
| Professional Fees | — | — | 1,076,276 |
| Clinical Trial Costs | 204,028 | 497,869 | 503,941 |
| Clinical Trial Materials | — | 341,775 | 352,734 |
| Dues and License Fees | 49,487 | 145,594 | 106,012 |
| Insurance | 144,525 | 163,284 | 118,936 |
| Rent | 214,764 | 27,778 | — |
| Other | 180,896 | 160,595 | 28,318 |
| | $ 1,212,183 | $ 1,961,243 | $ 2,816,413 |

**5. Property & Equipment, net:**

Property and equipment, net for the periods presented consist of the following:

| | December 31, 2016 | December 31, 2017 | March 31, 2018 |
|---|---|---|---|
| Leasehold Improvements | $ 2,203,282 | $ 10,873,895 | $ 11,284,844 |
| Manufacturing Equipment | — | 2,477,637 | 2,894,101 |
| Laboratory Equipment | 662,443 | 993,409 | 1,017,169 |
| Office Equipment | 100,350 | 276,100 | 282,172 |
| Asset Retirement Obligation | 205,659 | 153,133 | 158,044 |
| Furniture & Fixtures | 78,708 | 93,786 | 96,395 |
| | 3,250,442 | 14,867,960 | 15,732,725 |
| Less: Accumulated depreciation | (233,917) | (612,231) | (1,089,634) |
| | $ 3,016,525 | $ 14,255,729 | $ 14,643,091 |

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, $95,880 and $114,924 are included in office equipment at December 31, 2016 and 2017 and March 31, 2018, respectively, and accumulated depreciation of $6,928, $34,552 and $46,390 at December 31, 2016 and 2017 and March 31, 2018, respectively.

Depreciation expense was $243,081 and $679,177 for the years ended December 31, 2016 and 2017, respectively and $179,878 and $458,836 for the three months ended March 31, 2017 and 2018, respectively.

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**6. Restricted Cash:**

The Company is required to maintain stand-by letters of credit as security deposits under each of the ARE-East River Science Park LLC (“ARE”) leases (see Note 14). The fair value of each letter of credit approximates its contract value. In each case, the Company’s bank requires the Company to maintain restricted cash balances to serve as collateral for the letter of credit issued to the landlord by the bank. In connection with an amendment to one of the ARE leases in November 2017, the letter of credit in the amount of $321,978 and the related restricted cash balance were released in December 2017. As of December 31, 2016 and 2017 and March 31, 2018, the restricted cash balances for the ARE leases were invested in a commercial money market account.

The restricted cash balance for the other ARE lease remains at $123,376 through the end of the lease term in December 2021, plus three months.

The Company had $444,844, $123,376 and $123,376 of restricted cash included in long-term assets as of December 31, 2016 and 2017 and March 31, 2018, respectively and is measured using level 1 inputs.

Upon the retrospective adoption of ASU 2016-18 on January 1, 2018, as discussed in Footnote 2, restricted cash is now reflected in the beginning and ending balance of cash, cash equivalents and restricted cash for all periods presented in the Consolidated Statements of Cash Flows. As a result of this retrospective adoption, cash flows used in operating activities decreased by $441,049 and increased by $321,468 for the years ended December 31, 2016 and 2017, and $0 for the three month period ended March 31, 2017, respectively, resulting in revised net cash used in operating activities of $14,367,952 and $18,055,386 for the years ended December 31, 2016 and 2017, respectively, presented in the Consolidated Statements of Cash Flows.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the balance sheet that sum to the total of the same such amounts shown in the statement of cash flows:

| | December 31, 2016 | December 31, 2017 | March 31, 2018 |
|---|---|---|---|
| Cash and cash equivalents | $ 17,476,641 | $ 8,548,638 | $ 32,356,851 |
| Restricted cash | 444,844 | 123,376 | 123,376 |
| Total cash, cash equivalents and restricted cash shown in the statement of cash flows | $ 17,921,485 | $ 8,672,014 | $ 32,480,227 |

**7. Accrued Expenses:**

Accrued expenses for the periods presented were comprised of the following:

| | December 31, 2016 | December 31, 2017 | March 31, 2018 |
|---|---|---|---|
| Clinical Trial Costs | $ 664,149 | $ 4,859,410 | $ 4,243,611 |
| Compensation and Benefits | 1,418,958 | 2,386,903 | 390,896 |
| Consulting | 1,158,915 | 1,220,477 | 672,947 |
| Rent | 242,937 | 387,267 | 106,381 |
| Professional Fees | 323,102 | 231,923 | 910,081 |
| Interest | — | 33,437 | 25,500 |
| Other | 210,042 | 213,527 | 307,841 |
| | $ 4,018,103 | $ 9,332,944 | $ 6,657,257 |

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**8. Capitalized Leases:**

In 2015, the Company acquired certain office equipment in the amount of $17,817 under a 3-year lease arrangement. The Company determined that the lease should be capitalized since it contained a bargain purchase option for the equipment at the end of the lease term. Total payments under the capital lease amounted to $20,502 and had an interest rate of 9.35%.

In 2017, the Company acquired additional office equipment in the amount of $78,063 under a 3-year lease arrangement. The Company determined that the lease should be capitalized since it contained a bargain purchase option for the equipment at the end of the lease term. Total payments under the capital lease amounted to $86,145 and had an interest rate of 6.90%.

The following is a schedule, by year, of future minimum lease payments under the capital leases together with the present value of the net minimum lease payments as of December 31, 2016 and 2017 and March 31, 2018:

| | December 31, 2016 | December 31, 2017 | March 31, 2018 |
|---|---|---|---|
| 2018 | $ 6,834 | $ 34,410 | $ 25,523 |
| 2019 | 5,695 | 28,715 | 28,715 |
| 2020 | — | 7,179 | 7,179 |
| Total minimum lease payments | 12,529 | 70,304 | 61,417 |
| Less: amount representing interest | (1,056) | (5,156) | (4,047) |
| Present value of net minimum lease payments | 11,473 | 65,148 | 57,370 |
| Less: current portion | (6,015) | (30,850) | (28,715) |
| Obligations under capital lease, less current portion | $ 5,458 | $ 34,298 | $ 28,655 |

**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 15). 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. In March 2018, the Company repaid the note in full in cash. The Company recorded interest expense in the consolidated statement of operations and comprehensive loss in connection with the note in the amount of $13,037 and $17,386 for the year ended December 31, 2017 and for the three months ended March 31, 2018, respectively.

**10. Share-Based Compensation**

***2016 Equity Incentive Plan***

The Company’s 2016 Equity Incentive Plan (the “Plan”), was adopted by the Company’s board of directors and shareholders. Under the Plan, the Company has granted share options to selected officers, employees and non-employee consultants. The Company's board of directors administer the Plan. Options granted under the Plan have a maximum contractual term of ten years. Options granted generally vest 25% on the first anniversary date of grant and the balance ratably over the next 36 months.

A summary of the Company's share option activity related to employees, non-employee members of the board of directors and non-employee consultants as of and for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018 is as follows:

| | 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 |
| Granted | 2,622,500 | 1.45 | |
| Exercised | — | — | |
| Expired | — | — | |
| Forfeited | — | — | |
| Outstanding at March 31, 2018 | 6,265,500 | $ 1.37 | $ 1,867,400 |
| 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 | | |
| Weighted average remaining contractual life of options outstanding as of March 31, 2018 (yrs) | 9.22 | | |
| Options exercisable at December 31, 2016 | 125,000 | $ 1.99 | $ — |
| Options exercisable at December 31, 2017 | 723,398 | $ 1.99 | $ — |
| Options exercisable at March 31, 2018 | 912,854 | $ 1.98 | $ — |
| 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 | | |
| Weighted average remaining contractual life of options exercisable as of March 31, 2018 (yrs) | 8.07 | | |

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The total fair value of options vested during the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018, was $180,723, $898,699 and $309,147, respectively.

During the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018, the Company granted 915,000, 1,020,000 and 2,070,000 share options, respectively, to employees and non-employee members of the board of directors. The grant date fair values of the stock options granted to those groups were estimated using the Black-Scholes option valuation model with the following ranges of assumptions (see Note 2):

| | For the Year Ended December 31, | | For the Three Month Period Ended March 31, |
|---|---|---|---|
| | 2016 | 2017 | 2018 |
| Risk-free interest rate | 1.38% - 1.55% | 2.28% | 2.32% - 2.40% |
| Expected volatility | 90% | 90% | 90% |
| Expected dividend yield | 0% | 0% | 0% |
| Expected life of employee and Board of Directors’ options (in years) | 5.0 - 6.1 | 5.5 - 6.1 | 5.5 - 6.1 |

As of December 31, 2016 and 2017 and March 31, 2018, the total compensation expense relating to unvested options granted to employees and non-employee members of the board of directors that had not yet been recognized was $800,976, $987,413 and $2,912,830, respectively which is expected to be realized over a period of 3.17, 3.42 and 3.78 years, respectively. The Company will issue shares upon exercise of options from Ordinary Shares reserved.

During the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018, the Company granted 380,000, 1,355,000 and 552,500 share options, respectively to non-employee consultants. In accordance with ASC 505-50, on December 31, 2016 and 2017 and March 31, 2018, the Company remeasured the fair value, of all unvested outstanding options that had been granted to non-employee consultants using the Black-Scholes option valuation model with the following ranges of assumptions:

| | For the Year Ended December 31, | | For the Three Month Period Ended March 31, |
|---|---|---|---|
| | 2016 | 2017 | 2018 |
| Risk-free interest rate | 2.45% | 2.36% - 2.39% | 2.76% - 2.81% |
| Expected volatility | 90% | 90% | 90% |
| Expected dividend yield | 0% | 0% | 0% |
| Expected life of non-employee options (in years) | 9.2 - 10.0 | 8.2 - 9.7 | 7.9 - 9.8 |

As of December 31, 2016 and 2017 and March 31, 2018, the total compensation expense relating to unvested options granted to non-employee consultants that had not yet been recognized was $456,707, $1,629,019 and $2,130,007, respectively, which is expected to be realized over a period of 3.17, 3.72 and 3.78 years, respectively. The Company will issue shares upon exercise of options from Ordinary Shares reserved.

The weighted average grant date fair value of options granted to employees, non-employee members of the board of directors for their Board service and non-employee consultants during the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018 was $1.51, $0.80 and $1.12, respectively.

***Restricted Shares***

In 2015, in connection with certain service and consulting agreements, certain employees and a consultant were awarded an aggregate of 3,367,710 restricted Ordinary Shares and 750 restricted B ordinary shares, which restricted B ordinary shares were converted into restricted Ordinary Shares, of the Company. Such shares are subject to forfeiture over a three-year service period. The shares were valued at $1.99 and $2.00 per share and is included in loss from operations over the requisite service period.

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 |
| Vested during the three-month period ended March 31, 2018 | 266,403 | 532,364 |
| Non-vested at March 31, 2018 | 144,646 | $ 333,497 |

During the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018 the Company recognized total share-based compensation expense in the accompanying statements of operations and comprehensive loss as follows:

| | December 31, 2016 | December 31, 2017 | March 31, 2018 |
|---|---|---|---|
| Research and development | $ 1,995,594 | $ 2,374,899 | $ 842,962 |
| General and administrative | 811,367 | 584,832 | 3,432,774 |
| Total share based compensation | 2,806,961 | $ 2,959,731 | $ 4,275,736 |

The Company does not expect to realize any tax benefits from its share option activity or the recognition of share-based compensation expense because the Company currently has net operating losses and has a full valuation allowance against its deferred tax assets. Accordingly, no amounts related to excess tax benefits have been reported in cash flows from operations or cash flows from financing activities for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2018.

**11. Convertible Preferred C Shares and Shareholders' Deficit:**

***Registration Rights Related to Ordinary Shares and Preferred Shares***

Holders of Preferred Shares who hold not less than 3% of the Company's fully diluted shares and certain other shareholders have piggyback registration rights with respect to the Company's registration of its Ordinary Shares following an initial public offering, subject to certain exceptions.

***Drag-Along Rights Related to Ordinary and Preferred Shares***

Pursuant to the Company's articles of association, if the holders of at least 50% of the voting power of the Company wish to sell their Ordinary Shares and/or Preferred Shares, then such holders have the right to require all other holders to accept the offer made to the them and sell their Ordinary Shares and/or Preferred Shares on the same terms, subject to certain exceptions with respect to the Company's registration of its Ordinary Shares.

***Ordinary Shares***

*Voting Rights*

Each share is entitled to one vote.

*Redemption*

The shares are not redeemable.

*Transfers*

Transfers to an affiliate or member, as defined, are permitted. Otherwise, the Ordinary Shares may not be transferred without approval from the Company's board of directors. If the transfer is approved, the Company has the right to purchase any or all of the Ordinary Shares on the same terms and conditions. If the Company does not exercise its right to purchase the Ordinary Shares, then the other shareholders have the right to purchase the Ordinary Shares on a pro-rata basis.

*Tag-Along Rights*

Pursuant to the Company's articles of association, if Kadmon holds more than 15% of the fully diluted share capital and proposes to transfer more than 25% of the aggregate number of Ordinary Shares held by Kadmon and its affiliates to a third-party purchaser, before making such a transfer Kadmon must offer to all of the MeiraGTx UK II founders the right to purchase the same proportion of the Ordinary Shares held by each MeiraGTx UK II founder on the proportion of shares being sold by Kadmon and its affiliates, subject to certain exceptions with respect to the Company's registration of its Ordinary Shares.

*Right to Appointment of Board Member*

Pursuant to the Company's shareholders' agreement, as long as Kadmon's ownership percentage of the Company is at least 10%, Kadmon has the right to appoint a board member to the Company's board of directors. This right in the shareholders' agreement terminates upon an initial public offering.

*Issuances*

*2016*

On January 1, 2016, the Company issued 300,000 Ordinary Shares in connection with the BRI-Alzan acquisition described in Note 3.

On April 5, 2016, the Company issued 4,017,048 Ordinary Shares in connection with the acquisition of the remaining 40% of MeiraGTx UK II described in Note 2.

On April 7, 2016, the Company issued 46,300 Ordinary Shares in connection with a consulting agreement.

On July 7, 2016, all of the 10,000 B ordinary shares outstanding were converted into 10,000 Ordinary Shares.

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*2017*

On July 31, 2017, the Company issued 5,000 Ordinary Shares in connection with the exercise of an option.

On August 16, 2017, the Company issued 25,000 Ordinary Shares in connection with a research agreement.

*2018*

On March 1, 2018, a funding milestone was met under the employment agreements for certain senior management. Accordingly, the employees were issued an aggregate of 2,135,182 fully vested Ordinary Shares, which represented 3% of the fully-diluted outstanding shares of the Company as of such date. The shares were recorded as share-based compensation in the amount of $3,096,104. Additionally, under the terms of the employment agreements, the Company was required to pay the income taxes on those shares on behalf of the executives. Total compensation expense in connection with the issuance of these Ordinary Shares, in the amount of $6,154,608, was recorded as general and administrative expense during the three-month period ended March 31, 2018.

***Convertible Preferred C Shares***

*Redemption*

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

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

*Liquidation Preference*

The Preferred Shares contain a liquidation preference whereby on a return of assets on liquidation or capital reduction or otherwise, the surplus assets and retained profits of the Company available for distribution among the holders of Shares shall be applied:

- first in paying to the holders of Preferred Shares a sum equal to $2.70; and
- second, the balance of such assets (if any) shall be distributed amongst the holders of Ordinary Shares pro rata to the number of shares held by each of them respectively.

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In September 2017, the shareholders amended the Company's articles of incorporation to reduce the liquidation value of the Preferred Shares from $5.40 to $2.70. Concurrently, the board of directors approved a dividend of 6,149,326 Preferred Shares to the existing holders of 6,149,326 Preferred Shares that had previously been purchased from the Company at a liquidation value of $5.40 per share. The Company has accounted for this amendment as an extinguishment. The new Preferred Shares issued in connection with the extinguishment were recorded at fair value. The fair value of the newly issued Preferred Shares issued in connection with the extinguishment was determined based upon recent sales of the Company's Preferred Shares to third parties on or about the time of the extinguishment. The extinguishment and concurrent dividend resulted in $0.1 million of loss being added to loss available to ordinary shareholders for earning per share purposes. (see Note 12).

*Conversion*

The Preferred Shares may be converted by the holder into Ordinary Shares, on a one to one basis, at any time, subject to adjustment for share splits and share dividends. The Preferred Shares shall automatically be converted and reclassified as Ordinary Shares with effect from and immediately prior to the completion of a Qualified IPO.

*Dividends*

There are no dividends on the Preferred Shares.

*Voting Rights*

Each Preferred Share is entitled to one vote.

*Transfers*

Transfers to an affiliate or member, as defined, are permitted. Otherwise, the Preferred Shares may not be transferred without approval from the Company's board of directors. If the transfer is approved, the Company has the right to purchase any or all of the Preferred Shares on the same terms and conditions. If the Company does not exercise its right to purchase the Preferred Shares, then the other Preferred Shareholders has the right to purchase the Preferred Shares on a pro-rata basis.

*Pre-Emptive Rights*

The holders of the Preferred Shares have the right to participate in any new offering of equity shares in the same proportion as their holdings prior to the new offering.

*Tag-Along Rights*

If one or more of the holders proposes to transfer 15% or more of all shares issued by the Company, the transferee of the shares must offer to purchase from each holder of the Preferred Shares such proportion of the number of each class of shares registered in their name as is equal to the proportion which the shares that the transferor are proposing to transfer to the transferee.

*Right to Appointment of Board Member*

As long as Perceptive Life Sciences Master Fund, Ltd., holds not less than 50% of the Preferred Shares it owned on September 18, 2017 and April 12, 2018, it shall have the right to appoint a board member to the Company's board of directors, which it did on October 19, 2017. This right in the shareholders' agreement terminates upon an initial public offering.

*Issuances*

*2016*

During the year ended December 31, 2016, the Company issued 3,877,827 Preferred Shares at an offering price of $5.40 per share for proceeds of $20,770,031, net of issuance costs of $177,623. The net proceeds of the offering are being used for working capital, research and development and general corporate purposes.

In April 2016, the Company issued 230,000 Preferred Shares in the amount of $1,242,000 as partial payment for amounts due to Affiliate.

On December 20, 2016, the Company issued 59,259 Preferred Shares in connection with a license agreement described in Note 15.

*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 15).

*2018*

During the three-month period ended March 31, 2018, the Company issued 16,348,917 Preferred Shares at an offering price of $2.70 per share for gross proceeds of $44,142,076, excluding offering costs of $290,475.

Also, during the three-month period ended March 31, 2018, the Company issued 501,886 Preferred Shares in lieu of cash payment of an aggregate amount $1,355,097 to certain vendors.

On March 15, 2018, the Company issued 51,852 Preferred Shares in connection with a license agreement.

The net proceeds of the offering are being used for working capital, research and development and general corporate purposes.

***Warrants***

In connection with the issuance of 2,777,778 Preferred Shares on September 21, 2017, at an offering price of $2.70 per share, the Company issued warrants to purchase 2,700,000 Preferred Shares at an exercise price of $2.70 per share. The warrants expire on the first of the following to occur:

(i) an Asset Sale;
(ii) a Qualified IPO;
(iii) a Share Sale;
(iv) the winding up of the Company; or
(v) On the third anniversary of the date of issuance

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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 15).

The Black-Scholes value of the warrants in the amount of $553,500 was recorded as a warrant liability and charged to convertible note inducement expense within the statement operations and comprehensive loss at the time of issuance.

Both of the warrants were revalued under the Black-Scholes valuation model at December 31, 2017 and March 31, 2018, which resulted in an increase of the warrant liability in the amount of $465,633 and a decrease of the warrant liability in the amount of $669,408, respectively, which was charged to change in fair value of warrant liability within the statement of operations and comprehensive loss.

The warrant liability at December 31, 2017 and March 31, 2018 was $2,679,633 and $2,010,225, respectively.

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## 12. Net Loss per Share

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

| | For the Year Ended December 31, | |
|---|---|---|
| | 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) |

| | For the Three Month Period Ended March 31, | |
|---|---|---|
| | 2017 | 2018 |
| Net loss attributable to MeiraGTx ordinary shareholders - basic and diluted | $ (6,820,385) | $(16,403,353) |
| Accretion of Preferred Shares financing costs | (22,761) | (94,445) |
| Accretion of warrant | — | (570,273) |
| Adjusted net loss attributable to MeiraGTx ordinary shareholders - basic and diluted | $ (6,843,146) | $(17,068,071) |
| Weighted-average ordinary shares outstanding: | | |
| Basic and Diluted | 32,851,408 | 34,647,368 |
| Net loss per share: | | |
| Basic and Diluted | $ (0.21) | $ (0.49) |

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 |
| A restricted ordinary shares subject to forfeiture | 1,489,333 | 411,049 |
| Stock options | 1,295,000 | 3,643,000 |
| Warrants | — | 3,600,000 |
| | 8,895,589 | 27,082,086 |

| | March 31, 2017 | March 31, 2018 |
|---|---|---|
| Preferred Shares | 6,149,326 | 36,330,692 |
| A restricted ordinary shares subject to forfeiture | 1,222,930 | 144,646 |
| Stock options | 1,720,000 | 6,265,500 |
| Warrants | — | 3,600,000 |
| | 9,092,256 | 46,340,838 |

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**13. Pro Forma Net Loss Per Share (unaudited)**

The following table sets forth the computation of the Company's unaudited pro forma basic and diluted net loss per share:

| | Year Ended December 31,2017 | Three-Month Period Ended March 31, 2018 |
|---|---|---|
| Numerator: | | |
| Adjusted net loss attributable to MeiraGTx Limited ordinary shareholders | $ (31,851,498) | $(17,068,071) |
| Accretion on convertible preferred C shares | 806,963 | 664,718 |
| Change in fair value of warrant liability | 465,633 | (669,408) |
| Acceleration of vesting on restricted shares | (175,983) | — |
| Pro forma adjusted net loss attributable to MeiraGTx Limited ordinary shareholders | $ (30,754,885) | $(17,072,761) |
| Denominator: | | |
| Weighted-average number of ordinary shares outstanding | 33,269,157 | 34,647,368 |
| Pro forma adjustment to reflect the automatic conversion of convertible preferred C shares upon the closing of the proposed initial public offering | 36,330,692 | 36,330,692 |
| Pro forma adjustment to reflect to exercise of the warrants prior to the closing of the proposed initial public offering | 3,600,000 | 3,600,000 |
| Acceleration of vesting on restricted shares | 89,398 | 89,398 |
| Pro forma weighted-average number of ordinary shares outstanding | 73,289,247 | 74,667,458 |

**14. Income Taxes:**

Since the Company has recurring losses and a valuation allowance against deferred tax assets, there is no tax expense (benefit) for the years ended December 31, 2016 or 2017 and for the three month periods ended March 31, 2017 or 2018.

Each Company files separate tax returns in its respective tax jurisdictions.

As of December 31, 2017, the Company had federal and state net operating loss ("NOL") carryforwards in the United States of approximately $7,820,000 and $7,779,000, respectively, and in the United Kingdom of approximately $39,971,000, which are available to reduce future taxable income. The U.S. federal and state NOL carry forwards will begin to expire in 2035 and the U.K. NOL will continue indefinitely under current UK legislation. Also, as of December 31, 2017, the Company had research and development credits in the U.S. in the amount of $697,000. The NOL carry forwards are subject to review and possible adjustment by the U.S., U.K. and state tax authorities. NOL carry forwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders, as defined under Sections 382 Internal Revenue Code, as well as CTA 2010 Part 14 under the UK tax rules. This could limit the amount of NOLs that the Company can utilize annually to offset future taxable income or tax liabilities. As of December 31, 2017, the Company has not performed such an analysis. Subsequent ownership changes and proposed future changes to the UK (or US) tax rules in respect of the utilization of losses carried forward may further affect the limitation in future years. Additionally, the Company has not undertaken a study on the completeness of the U.S. research and development credit. As such, the U.S. research and development credits may change.

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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 UK Rate Change (17% at expected DTA turn) | 582,910 | -2.95% | 482,351 | -1.55% |
| Federal & State Rate Change (Jobs Act & MTA) | — | 0.00% | 993,998 | -3.20% |
| Change in valuation allowance | 3,516,208 | -17.77% | 4,942,855 | -15.92% |
| Actual income tax benefit effective tax rate | — | 0.00% | — | 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) | — | — |

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***Deferred Tax Assets/(Liabilities)***

| | 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 | $ 9,462,690 | $ 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.

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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.

**15. Related Party Transactions:**

***Transition Services Agreement***

Effective April 24, 2015, the Company entered into a transition services agreement (the "TSA") with Kadmon, whereby Kadmon would provide office and laboratory facilities as well as certain other personnel support activities to the Company. Under the agreement, the Company is charged for (i) rent based upon the square footage of the office and laboratory facilities used by the Company (ii) other personnel support activities based upon the hours of the personnel providing the support activities, and (iii) and other direct costs incurred by Kadmon on behalf of the Company, plus a 7% administrative fee. The TSA may be terminated by either party by giving thirty-days' notice.

During the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, the Company incurred the following charges in connection with the TSA and is included in loss from operations:

| | Years Ended December 31, | | Three Months Ended March 31, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| Rent | $ 794,087 | $548,229 | $ 123,355 | $ 136,353 |
| Personnel | 189,104 | 39,721 | 18,532 | 6,493 |
| Other | 42,110 | 5,983 | 5,080 | — |
| Total charges incurred | $1,025,301 | $593,933 | $ 146,967 | $ 142,846 |

During the year ended December 31, 2016 and 2017, the Company made cash payments totaling $225,078 and $275,941, respectively. During the three-month periods ended March 31, 2017 and 2018, the Company made cash payments totaling $275,941 and $997,417, respectively. Additionally, in April 2016, as partial payment of the amounts owed to Kadmon, the Company issued 230,000 Preferred Shares in the amount of $1,242,000.

The amount due to Kadmon at December 31, 2016 and 2017 and March 31, 2018, is $543,038, $861,030, and $6,493, respectively and is disclosed as Due to Kadmon on the balance sheet.

***Research Agreement***

Effective October 23, 2016, the Company entered into a four-year master services agreement with UCL Consultants Limited, an entity affiliated with University College of London ("UCL"), which is a shareholder of the Company. Pursuant to the agreement, UCL Consultants Limited provides pre-clinical research and development under the direction of the Company. In connection with the agreement, the Company issued several work orders during the years ended December 31, 2016 and 2017 in the aggregate amounts of £1,161,149 and £241,053, respectively, or approximately $1,574,000 and $311,000, based upon the average exchange rates during the years ended December 31, 2016 and 2017, respectively. Either party may terminate the agreement by giving 30 days written notice. Total research and development expenses under this agreement for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018 was approximately $278,000 and $538,000, and $108,000 and $189,000, respectively. Future obligations, under the agreement equal £927,823, or approximately $1,301,921 through October 2020.

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The amount due to UCL under the master services agreement at December 31, 2016 and 2017 and March 31, 2018, is $251,754, $775,315 and $377,145, respectively and is included in accounts payable and accrued expenses on the balance sheet.

***Manufacturing Agreement***

Effective September 1, 2016, the Company entered into a manufacturing and drug supply agreement with UCL. Pursuant to the agreement, UCL will manufacture materials for the Company's clinical trials under the direction of the Company. Either party may terminate the agreement by giving 30 days written notice. The agreement was terminated in January 2018. Total research and development expenses under this agreement for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, was approximately $456,106 and $1,904,352, and $563,024 and $0, respectively.

The amount due to UCL under the manufacturing and drug supply agreement at December 31, 2016 and 2017 and March 31, 2018, is $412,395, $2,466,142 and $2,545,226, respectively and is included in accrued expenses on the balance sheet.

***Leases***

*July 2016 Lease*

Effective July 1, 2016, the Company entered into a non-cancellable operating lease for laboratory and related office facilities in New York with ARE, an entity that is under common control by an entity that is a minority shareholder of the Company and whose CEO is a director of the Company. The lease provides for monthly base rent and property management fees, including rent escalations and rent holidays, plus operating expenses during the lease term, which expires on December 31, 2021. The Company records monthly rent expense on a straight-line basis from July 1, 2016 through December 31, 2021. As of December 31, 2016 and 2017 and March 31, 2018, the balance of deferred rent, representing the difference between cash rent paid and straight-line rent expense, was $243,780, $231,276 and $225,999, respectively.

Total rent expense under this operating lease was $243,780 and $487,559 for the years ended December 31, 2016 and 2017, respectively, and $121,890 for the three months ended March 31, 2017 and 2018. As of March 31, 2018, the aggregate future minimum rental payments under this lease are $2,054,343.

In connection with the signing of this lease, the Company entered into a standby letter of credit agreement for $122,866, which serves as a security deposit for the premises. The standby letter of credit expires on July 7, 2017 and is automatically renewed annually through July 7, 2021. This standby letter of credit is secured with restricted cash in a money market account (see Note 6).

*December 2016 Lease*

Effective December 15, 2016, the Company entered into another non-cancellable operating lease with ARE, expiring on October 31, 2032, for laboratory and office facilities in New York. The lease provided for monthly base rent, including rent escalations, property management fees and rent holidays, plus operating expenses during the lease term. The Company recorded monthly rent expense on a straight-line basis from December 15, 2016 through October 31, 2032. On October 26, 2017, the lease was amended, whereby the lease would terminate on March 31, 2018 and only base rent and management fees in the aggregate amount of $563,507 would be due from November 1, 2017 through March 31, 2018. Under the amendment, the Company issued a note to ARE in the amount of $1,442,009 (see Note 9), removed the balance of the deferred rent and accrued the future rent payments, all of which were recorded as rent expense at the time of the amendment, in accordance with ASC 420, Exit and Disposal Activities, as the Company had a cease use date as of the date of the amendment. As of December 31, 2016 and 2017 and March 31, 2018, the balance of deferred lease obligation, representing the difference between cash rent paid and straight-line rent expense, was $11,380, $0 and $0, respectively.

Total rent expense under this operating lease was $43,578 and $1,660,806 for the years ended December 31, 2016 and 2017, and $390,903 and $0 for the three months ended March 31, 2017 and 2018, respectively.

On October 26, 2017, in connection with the amendment to the lease, the Company issued a promissory note in the amount of $1,442,009 to ARE. The note accrued interest at the rate of 5% per annum and was due on December 31, 2018. However, if the Company had sufficient liquidity, as defined in the note, then the note, including accrued interest, would become due and payable at that time. In accordance with the sufficient liquidity provision, the Company repaid the note, plus accrued interest, in the aggregate amount of $1,472,433 during the three-month period ended March 31, 2018.

The Company recorded interest expense in the consolidated statement of operations and comprehensive loss in connection with the note in the amount of $17,387 for the three-month period ended March 31, 2018.

***Convertible Note Payable***

On May 1, 2017, the Company issued a convertible note in the amount of $2,500,000 to ARE. The note had an interest at a rate of 10% per annum and was convertible into Preferred Shares at any time at the option of the holder or would automatically convert into Preferred Shares in the event of an equity investment by a mutually agreed upon institutional investor at a price per share equal to the lowest price paid per share by a purchaser of the Company’s Preferred Shares. On November 2, 2017 the note was converted to 925,926 Preferred Shares at $2.70 per share. In accordance with the terms of the convertible note, the accrued interest in the amount of $145,833 was cancelled.

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).

**16. Commitments:**

***Operating Leases***

In February 2016, the Company entered into a non-cancellable operating lease, expiring in February 2021, for manufacturing and office facilities in London, UK. The lease provides for an additional five-year term at the Company’s option. The lease provides for monthly base rent, plus operating expenses and real estate taxes during the lease term.

In connection with a provision in the lease requiring the Company to remove all equipment and leasehold improvements upon the termination of the lease, the Company estimated that it had an asset retirement obligation at the end of the lease term in the amount of $306,400. The Company discounted the asset retirement obligation using an 8% discount rate and recorded an asset retirement obligation in the amount of $205,659, which is included in leasehold improvements. As of December 31, 2017, the Company determined that it will more likely than not exercise the additional five-year option provided for in the operating lease. Therefore, the company revalued the asset retirement obligation over the remaining eight-year lease term and recorded a reduction in the asset retirement obligation of $75,011. During the years ended December 31, 2016 and 2017, and the three months ended March 31, 2017 and 2018, the Company recorded $17,247 and $7,571 and $4,685 and $3,678 of interest expense, respectively. The carrying value of the asset retirement obligation at December 31, 2016 and 2017 and March 31, 2018 is $221,254, $178,419 and $187,848, respectively. Total rent expense under this operating lease was $266,698 and $279,303 for the years ended December 31, 2016 and 2017, respectively, and $67,259 and $74,001 for the three months ended March 31, 2017 and 2018, respectively.

On October 1, 2017, the Company entered into a one-year non-cancellable operating lease, expiring in September 2018, for office and laboratory facilities in Leiden, Netherlands. The lease provides for monthly base rent plus operating expenses during the lease term. The lease provides for successive one-year extensions up to a maximum of four extensions. Total rent expense under this operating lease was $0 and $5,273 for the years ended December 31, 2016 and 2017, respectively, and $0 and $2,703 for the three months ended March 31, 2017 and 2018, respectively.

In June 2017, the Company entered into two non-cancellable operating leases, expiring in July 2018, for office facilities in London, UK. The lease provides for monthly base rent, rent holidays plus operating expenses and real estate taxes during the lease term. The Company records monthly rent expense on a straight-line basis from June 1, 2017 through July 23, 2018. As of December 31, 2017 and March 31, 2018, the balance of deferred lease obligation, representing the difference between cash rent paid and straight-line rent expense, was $35,014 and $15,489, respectively. Total rent expense under theses operating leases was $0 and $85,222 for the years ended December 31, 2016 and 2017, respectively, and $0 and $27,774 for the three months ended March 31, 2017 and 2018, respectively.

The aggregate future minimum rental payments under these leases as of December 31, 2017 are as follows:

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

The aggregate future minimum rental payments of all leases, including those discussed in Note 14, as of December 31, 2017 are as follows:

| | |
|---|---|
| 2018 | $1,215,723 |
| 2019 | $ 828,813 |
| 2020 | $ 847,562 |
| 2021 | $ 598,264 |
| Total future rent payments | $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 at any time by either party by giving twelve-months' notice, or the Company may terminate the officer's employment effective immediately upon notice, and within 28 days making payment in lieu of notice consisting of a sum equivalent to the officer's annual salary for the relevant period. For the years ended December 31, 2016 and 2017, the Company recorded £430,000 and £724,000 or approximately $583,000 and $933,000, respectively, using the average exchange rates during the year ended December 31, 2016 and 2017, respectively, in research and development costs under these agreements. For the three months ended March 31, 2017 and 2018, the Company recorded £83,000 and £103,000 or approximately $102,000 and $145,000, respectively, using the average exchange rates during the three months ended March 31, 2017 and 2018, respectively, in research and development costs under these agreements. Future obligations to be paid under these agreements equal £34,000, or approximately $48,000, using exchange rates as of March 31, 2018.

In connection with the service agreements, on April 24, 2015, the employees were awarded, under a share award agreement, an aggregate of 2,704,800 restricted Ordinary Shares and 750 B ordinary shares, which B ordinary shares have been converted into Ordinary Shares of the Company. Under the Share Award Agreement, such shares are subject to forfeiture ratably over a period of three years if the employee's do not remain an employee or consultant to the Company. The shares were valued at $2.00 per share and, in accordance with ASC718, are being charged to operations as stock compensation ratably over the forfeiture period.

***Employment Agreements***

In February 2016, the Company entered into three-year employment agreements with certain senior officers of the Company. Under the terms of the agreements, the employees will receive annual compensation in the aggregate amount of $710,000, which was increased to a maximum aggregate amount of $1,075,000. The employment agreements also provide for an annual guaranteed cash bonus targeted at 100% of annual compensation. The agreements also provide for discretionary annual performance bonuses targeted to be not less than 50-60% of the employee's base salary and grants of restricted stock. In January 2018 the Company's compensation committee approved a discretionary bonus in the aggregate amount of $1,196,000. This discretionary bonus and the guaranteed bonus for 2017, in the amount of $850,000, are subject to compensation committee approval and meeting certain future funding conditions. On February 28, 2018, the funding conditions were met.

Additionally, the agreements provide for equity incentives of up to an aggregate a maximum of 8.0% of the Company's fully diluted outstanding shares upon the attainment of certain milestones. On March 1, 2018, a funding milestone was met. Accordingly, the employees were issued an aggregate of 3% of the fully-diluted outstanding shares of the Company as of such date. (see Note 17).

The employees are also entitled to participate in all incentive and deferred compensation and employee benefit programs available to employees and executive officers of the Company. Future obligations to be paid under these agreements equal $1,881,250, as of March 31, 2018.

***Consulting and other Agreements***

Effective September 28, 2015, the Company entered into a three-year consulting agreement with a consultant to provide ongoing strategic advice and to serve on the Company's board of directors. In connection with the agreement, the Company issued 662,910 restricted Ordinary Shares. Under the consulting agreement, such shares are subject to forfeiture ratably over a period of three years if the consultant does not remain a consultant to the Company. The shares were valued at $1.99 per share and are being charged to general and administrative expenses upon the expiration of each forfeiture period.

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***Research Agreements***

On April 24, 2015, the Company entered into a cooperative research and development agreement (CRADA) with the U.S. Department of Health & Human Services, as represented by the National Institute of Dental and Craniofacial Research (NIDCR) and Institute or Center of the National Institutes of Health (NIH). The CRADA provided for quarterly payments of $21,250 for three years through April 30, 2017 and a cost per patient for each patient enrolled in the Company's xerostomia clinical trial. The CRADA was amended on March 25, 2016 to extend the term through March 25, 2021 and to extend the annual payments throughout the revised term. Research and development expenses under the CRADA for the year ended December 31, 2016 and 2017 were $76,161 and $115,374, respectively, and for the three months ended March 31, 2017 and 2018 were $25,002 and $28,348, respectively. Future obligations to be paid under the CRADA, as amended, through March 25, 2021 equal $255,000.

On March 22, 2016, the Company entered into a five-year cooperative research and development agreement (CRADA) with the U.S. Department of Health & Human Services, as represented by the National Institute of Dental and Craniofacial Research (NIDCR) and Institute or Center of the National Institutes of Health (NIH) for the treatment of Sjogren's Syndrome associated salivary hypofunction. The CRADA provides for quarterly payments of $104,500 for the first three years of the agreement plus a cost per patient for each patient enrolled in a clinical trial. The costs associated with years four and five of the CRADA will be determined at a later date. Total research and development expenses under this agreement for the years ended December 31, 2016 and 2017 and the three months ended March 31, 2017 and 2018, were $325,343, $418,000, $104,500 and $104,500, respectively. Future obligations to be paid under the agreement through March 22, 2019 equal $313,500.

Effective December 5, 2016, the Company entered into a three-year research collaboration agreement with Cornell University. Pursuant to the agreement, Cornell University provides research and development under the direction of the Company. In connection with the agreement, in July 2017, the Company issued 25,000 Ordinary Shares to Cornell University, which were recorded as research and development expenses in the amount of $17,000. The Company amended this agreement effective June 12, 2017 to add a second three-year research collaboration project through September 2019. Total research and development expenses under this agreement, as amended, for the years ended December 31, 2016 and 2017 and for the three months ended March 31, 2017 and 2018, were $63,337 and $1,029,904, and $190,011 and $448,173, respectively. Future obligations to be paid under the agreement through December 5, 2019 equal $2,898,602.

On February 14, 2017, the Company entered into a one-year research collaboration agreement with Cornell University in the amount of $679,473. On August 24, 2017, the agreement was amended to add an additional study in the amount of $182,520. Total research and development expenses under this agreement for the years ended December 31, 2016 and 2017 and for the three months ended March 31, 2017 and 2018, were $0 and $698,307, and $91,401 and $77,177, respectively.

***License Agreements***

Effective February 4, 2015, the Company entered into an exclusive worldwide license agreement with UCL Business, PLC ("UCL Business"), an entity that employs the Company's Chief Scientific Officer, to develop up to eight programs using certain ocular gene therapy technology. Under the terms of the agreement, as amended, the Company will pay UCL Business certain sales milestone payments, if achieved, in the aggregate amount of £39.8 million, or approximately $54.0 million using the exchange rate at December 31, 2017, and royalties on net sales, as defined upon commercialization. Additionally, the Company is responsible for all patent prosecution and maintenance costs incurred and will also pay UCL Business an annual maintenance fee of

£50,000, or approximately $68,000, until the first commercial sale of a product. The agreement will terminate upon the later of (i) the last valid claim in a relevant product (ii) the expiration of regulatory exclusivity to all licensed products, or (iii) the 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, and the three months ended March 31, 2017 and 2018, were $67,775 and $73,250, and $61,996 and $79,738, respectively.

On July 28, 2017, the Company entered into another worldwide license agreement with UCL Business for an additional program using certain ocular gene therapy technology. The Company will pay UCL Business certain milestone payments, royalties and annual maintenance fees under the same terms and conditions as the license dated February 4, 2015. Total research and development expenses under the agreement for the years ended December 31, 2016 and 2017, and the three months ended March 31, 2017 and 2018, were $0, $82,260 and $0, respectively.

Effective March 15, 2018, the Company entered into a third exclusive worldwide license agreement with UCL Business for an additional program using certain ocular gene therapy technology. The Company issued 51,852 Preferred Shares to UCL Business, which were recorded as research and development expenses in the amount of $140,000 during the three-month period ended March 31, 2018, and will pay UCL Business certain milestone payments, royalties and annual maintenance fees under the same terms and conditions as the license dated February 4, 2015. The Company did not incur any additional research and development expenses under the agreement during the three-month period ended March 31, 2018.

Effective January 1, 2016, the Company entered into an Agreement (“Agreement”) and Plan of Merger to acquire all of the outstanding shares of BRI-Alzan from the shareholders of BRI-Alzan. In connection with the Agreement, the Company will pay certain development milestone payments if achieved, in the aggregate amount of $4.5 million, and annual royalty payments on annual net sales following the first commercial sale of any product containing the technology acquired (see Note 3).

**17. 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.

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Under the HMRC requirements, current required minimum employer contributions are 2-3% but will rise to between 5-6% after April 2018 and 8-9% after April 2019.

During the years ended December 31, 2016 and 2017, and three months ended March 31, 2017 and 2018, employer contributions to all plans were $128,281, $252,700, $73,838 and $147,566, respectively.

**18. Subsequent Events:**

Management has evaluated subsequent events through the date of this filing. Based on our evaluation, the following disclosures have been made:

***Preferred Shares***

From April 1, 2018 through April 30, 2018, the Company issued 4,706,495 Preferred Shares at an offering price of $2.70 per share for gross proceeds in the amount of $12,707,536.

Through and including            , 2018 (the 25th day after the date of this prospectus), all dealers effecting transactions in the ordinary shares, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

# 5,000,000 Shares

MEIRAGTx

## Ordinary Shares

**PROSPECTUS**

## 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 | $ 11,454 |
| FINRA filing fee | 14,800 |
| Nasdaq fee | 200,000 |
| Accountants’ fees and expenses | 500,000 |
| Legal fees and expenses | 1,825,000 |
| Blue Sky fees and expenses | 15,000 |
| Transfer Agent’s fees and expenses | 10,000 |
| Printing and engraving expenses | 100,000 |
| Miscellaneous | 73,746 |
| Total expenses | $ 2,750,000 |

### Item 14. Indemnification of Directors and Officers.

Cayman Islands law does not limit the extent to which a company’s amended and restated memorandum and articles of association may provide for indemnification of officers and directors, except to the extent any such provision may be held by the Cayman Islands courts to be contrary to public policy, such as to provide indemnification against civil fraud or the consequences of committing a crime. Our amended and restated memorandum and articles of association, which will become effective upon the completion of this offering, provide that our board of directors and officers shall be indemnified from and against all liability which they incur in execution of their duty in their respective offices, except liability incurred by reason of such directors’ or officers’ dishonesty, willful default or fraud.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is theretofore unenforceable.

Our amended and restated memorandum and articles of association will provide:

“Every Director (including for the purposes of this Article any alternate Director appointed pursuant to the provisions of these Articles), Secretary, assistant Secretary, or other Officer (but not including the Company’s auditors) and the personal representatives of the same (each an “Indemnified Person”) shall be indemnified and secured harmless against all actions, proceedings, costs, charges, expenses, losses, damages or liabilities incurred or sustained by such Indemnified Person, other than by reason of such Indemnified Person’s own dishonesty, willful default or fraud as determined by a court of competent jurisdiction, in or about the conduct of the Company’s business or affairs (including as a result of any mistake of judgment) or in the execution or discharge of his duties, powers, authorities or discretions, including without prejudice to the generality of the foregoing, any costs, expenses, losses or liabilities incurred by such Indemnified Person in defending (whether successfully or otherwise) any civil proceedings concerning the Company or its affairs in any court whether in the Cayman Islands or elsewhere.

139. No Indemnified Person shall be liable:

(a) for the acts, receipts, neglects, defaults or omissions of any other Director or Officer or agent of the Company; or

(b) for any loss on account of defect of title to any property of the Company; or

(c) on account of the insufficiency of any security in or upon which any money of the Company shall be invested; or

(d) for any loss incurred through any bank, broker or other similar Person; or

(e) for any loss occasioned by any negligence, default, breach of duty, breach of trust, error of judgement or oversight on such Indemnified Person's part; or

(f) for any loss, damage or misfortune whatsoever which may happen in or arise from the execution or discharge of the duties, powers, authorities, or discretions of such Indemnified Person's office or in relation thereto;

unless the same shall happen through such Indemnified Person's own dishonesty, willful default or fraud as determined by a court of competent jurisdiction."

We intend to enter into indemnification agreements with each of our directors and officers. These indemnification agreements may require us, among other things, to indemnify our directors and officers for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of our directors or officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request.

We maintain a general liability insurance policy that covers certain liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of ordinary shares being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended, or the Securities Act, against certain liabilities.

**Item 15. Recent Sales of Unregistered Securities.**

Set forth below is information regarding shares of capital stock issued by us within the past three years. Also included is the consideration received by us for such shares and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of Capital Stock.

From April 24, 2015 through March 2, 2018, the registrant issued an aggregate (i) 1,050,831 Series A Ordinary Shares for aggregate consideration of approximately $8.7 million, (ii) 5,611,791 Series A Ordinary Shares for nominal consideration to the registrant's founders, (iii) 1,823,569 Series A Ordinary Shares in connection with acquisitions for aggregate consideration of approximately $14.2 million, (iv) 182,738 Series A Ordinary Shares in connection with consulting agreements for aggregate consideration of approximately $1.4 million, (v) 697,126 Series A Ordinary Shares in connection with service agreements for aggregate consideration of approximately $5.4 million and (vi) 9,017 Series A Ordinary Shares in connection with license agreements for aggregate consideration of approximately $52,000, to accredited investors, all pursuant to section 4(a)(2) of the Securities Act and Rule 506 as transactions not involving a public offering.

On July 24, 2017, the registrant issued 1,288 Series A Ordinary Shares pursuant to stock options exercised by an employee in connection with services provided to the registrant by the employee pursuant to Section 4(a)(2) and Rule 701 of the Securities Act as transactions not involving a public offering.

From October 1, 2015 through April 12, 2018, the registrant issued an aggregate (i) 10,291,361 Series C Preferred Shares for aggregate consideration of approximately $107.8 million, including $1.4 million in converted payables and $1.2 million of transitions services rendered, (ii) 238,579 Series C Preferred Shares in converted promissory notes upon the cancellation of principal debt totaling $2.5 million principal plus $145,933 accrued interest, and (iii) 43,898 Series C Preferred Shares in connection with research and license agreements for aggregate consideration approximately $0.5 million pursuant to Section 4(a)(2) and Rule 506 of the Securities Act.

(b) Equity Grants.

From March 4, 2016 through January 10, 2018, the registrant granted stock options to purchase an aggregate of 1,621,360 Series A Ordinary Shares with exercise prices ranging between $2.64 and $7.72 per share to employees, non-employee consultants, and directors in connection with services provided to the registrant by such parties pursuant to Section 4(a)(2) and Rule 701 of the Securities Act.

(c) Warrants.

On September 22, 2017, the registrant issued a warrant to purchase up to an aggregate of 695,696 shares of Series C preferred shares to Perceptive Life Sciences Master Fund, Ltd pursuant to Section 4(a)(2) and Rule 506 of the Securities Act as a transaction not involving a public offering.

On November 2, 2017, the registrant issued a warrant to purchase up to aggregate of 231,898 shares of Series C preferred shares to Alexandria Equities No. 7, LLC pursuant to Section 4(a)(2) and Rule 506 of the Securities Act as a transaction not involving a public offering.

(d) Issuance of Notes.

On May 1, 2017, the registrant issued a convertible note to an entity affiliated with Alexandria Equities No. 7, LLC, in the principal amount of $2.5 million pursuant to Section 4(a)(2) and Rule 506 of the Securities Act. On November 2, 2017, the convertible note was converted and the registrant issued 238,579 Series C preferred shares to Alexandria Equities No. 7, LLC at $10.48 per share for an aggregate consideration of approximately $2.5 million.

On October 26, 2017, the registrant issued a promissory note to Alexandria Equities No. 7, LLC in the principal amount of approximately $1.4 million pursuant to Section 4(a)(2) and Rule 506 of the Securities Act.

**Item 16. Exhibits and Financial Statement Schedules.**

(a) Exhibits.

| Exhibit Number | Description of Exhibit |
|---|---|
| 1.1 | Form of 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 consummation of the Corporate Reorganization) |
| 3.3 | Form of Restated Articles of Association of the Registrant (to be effective upon the closing of this offering) |
| 4.1** | Specimen Share Certificate evidencing the ordinary shares of the Registrant |
| 4.2 | Form of Shareholder Agreement (to be effective upon consummation of the Corporate Reorganization) |
| 5.1** | Opinion of Walkers |
| 10.1#** | 2016 Equity Incentive Plan, as amended, and form of option agreements thereunder |
| 10.2#** | 2018 Incentive Award Plan and forms of award agreements thereunder |
| 10.3#** | Non-Employee Director Compensation Program |
| 10.4#** | Form of Indemnification Agreement for Directors and Officers |
| 10.5** | Lease Agreement, dated June 29, 2016, as amended, between MeiraGTx Limited and ARE-East River Science Park LLC |
| 10.6** | Lease Agreement, effective February 2, 2016, among MeiraGTx Limited, 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., as amended |
| 10.8#** | Employment Agreement, dated February 15, 2016 between MeiraGTx Limited and Richard Giroux, as amended |
| 10.9#** | Employment Agreement, dated April 27, 2015, between MeiraGTx Limited and Stuart Naylor, Ph.D., as amended |
| 10.10†** | License Agreement, dated May 1, 2013, as amended, among MeiraGTx Limited, Brandeis University and BRI-Alzan Inc. |
| 10.11†** | License Agreement, dated February 4, 2015, as amended, between Athena Vision Ltd. and UCL Business, Plc |
| 10.12†** | License Agreement, dated July 28, 2017, as amended, between MeiraGTx UKII Limited and UCL Business, Plc |
| 10.13†** | License Agreement, dated March 15, 2018, among MeiraGTx Limited, MeiraGTx UKII-Limited and UCL Business Plc |
| 10.14†** | Agreement and Plan of Merger, dated December 31, 2015, among MeiraGTx Acquisition Corporation, BRI-Alzan, Inc., F-Prime Inc., Gregory Petsko, Dagmar Ringe, Brandeis University and MeiraGTx Limited |
| 10.15#** | 2018 Employee Share Purchase Plan |
| 21.1** | Subsidiaries of the Registrant |
| 23.1 | Consent of Ernst & Young LLP |
| 23.3** | Consent of Walkers (included in Exhibit 5.1) |
| 24.1** | Power of Attorney (included on signature page) |

* To be filed by amendment.
** Previously filed.
\# 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.

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## 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 4th day of June, 2018.

MeiraGTx Holdings plc

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

## SIGNATURES

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 |
|---|---|---|
| /s/ Alexandria Forbes, Ph.D.<br>Alexandria Forbes, Ph.D. | President, Chief Executive Officer and Director (principal executive officer) | June 4, 2018 |
| /s/ Richard Giroux<br>Richard Giroux | Chief Operating Officer<br>(principal financial officer and principal accounting officer) and MeiraGTx Holdings plc's authorized representative in the United States | June 4, 2018 |
| *<br>Keith R. Harris, Ph.D. | Chairman of the Board of Directors | June 4, 2018 |
| *<br>Ellen Hukkelhoven, Ph.D. | Director | June 4, 2018 |
| *<br>Arnold J. Levine, Ph.D. | Director | June 4, 2018 |
| *<br>Joel S. Marcus | Director | June 4, 2018 |
| *<br>Neil Mendoza | Director | June 4, 2018 |
| *<br>Gregory S. Moss | Director | June 4, 2018 |
| *<br>Stuart Naylor, Ph.D. | Director | June 4, 2018 |
| *<br>Thomas E. Shenk, Ph.D. | Director | June 4, 2018 |

*By: /s/ Richard Giroux
Attorney-in-fact

**Exhibit 1.1**

MeiraGTx Holdings plc

(a Cayman Islands exempted company)

[•] Ordinary Shares

UNDERWRITING AGREEMENT

Dated: June [•], 2018

MeiraGTx Holdings plc

(a Cayman Islands exempted company)

[•] ordinary shares, nominal value $[•] per share

**UNDERWRITING AGREEMENT**

June [•], 2018

Merrill Lynch, Pierce, Fenner & Smith
Incorporated

Barclays Capital Inc.

as Representatives of the several Underwriters

c/o Merrill Lynch, Pierce, Fenner & Smith
Incorporated

One Bryant Park
New York, New York 10036

c/o Barclays Capital Inc.
745 Seventh Avenue
New York, New York 10019

Ladies and Gentlemen:

Each of MeiraGTx Holdings plc, (a Cayman Islands exempted company) (the "Company") and MeiraGTx Limited, a private limited company organized under the laws of England and Wales ("MeiraGTx UK") confirms its respective agreement with each of the Underwriters named in Schedule A hereto (collectively, the "Underwriters," which term shall also include any underwriter substituted as hereinafter provided in Section 10 hereof), for whom Merrill Lynch, Pierce, Fenner & Smith Incorporated ("Merrill Lynch") and Barclays Capital Inc. are acting as representatives (in such capacity, the "Representatives"), with respect to (i) the issue and sale by the Company and the subscription by the Underwriters, acting severally and not jointly, of the respective numbers of ordinary shares, nominal value $0.00003881 per share, of the Company ("Ordinary Shares") set forth in Schedule A hereto and (ii) the grant by the Company to the Underwriters, acting severally and not jointly, of the option described in Section 2(b) hereof to subscribe for all or any part of [•] additional Ordinary Shares. The aforesaid [•] Ordinary Shares (the "Initial Securities") to be subscribed for by the Underwriters and all or any part of the [•] Ordinary Shares subject to the option described in Section 2(b) hereof (the "Option Securities") are herein called, collectively, the "Securities."

The Company understands that the Underwriters propose to make a public offering of the Securities as soon as the Representatives deem advisable after this Agreement has been executed and delivered.

The Company has filed with the Securities and Exchange Commission (the "Commission") a registration statement on Form S-1 (No. 333-224914), including the related preliminary prospectus or prospectuses, covering the registration of the sale of the Securities under the Securities Act of 1933, as amended (the "1933 Act"). Promptly after execution and delivery of this Agreement, the Company will prepare and file a prospectus in accordance with the provisions of Rule 430A ("Rule 430A") of the rules and regulations of the Commission under the 1933 Act (the "1933 Act Regulations") and Rule 424(b) ("Rule 424(b)") of the 1933 Act Regulations. The information included in such prospectus that was omitted from such registration statement at the time it became effective but that is deemed to be part of such registration statement at the time it became effective pursuant to Rule 430A(b) is herein called the "Rule 430A Information." Such registration statement, including the amendments thereto, the exhibits thereto and any schedules thereto, at the time it became effective, and including the Rule 430A Information, is herein called the "Registration Statement." Any registration statement filed pursuant to Rule 462(b) of the 1933 Act Regulations is herein called the "Rule 462(b) Registration Statement" and, after such filing, the term "Registration Statement" shall include the Rule 462(b) Registration Statement. Each prospectus used prior to the effectiveness of the Registration Statement, and each prospectus that omitted the Rule 430A Information that was used after such effectiveness and prior to the execution and delivery of this Agreement, is herein called a "preliminary prospectus." The final prospectus, in the form first furnished to the Underwriters for use in connection with the offering of the Securities, is herein called the "Prospectus." For purposes of this Agreement, all references to the Registration Statement, any preliminary prospectus, the Prospectus or any amendment or supplement to any of the foregoing shall be deemed to include the copy filed with the Commission pursuant to its Electronic Data Gathering, Analysis and Retrieval system or any successor system ("EDGAR").

On the date hereof, the business of the Company is conducted through MeiraGTx UK. Prior to the Closing Time (as defined below), the Company will acquire all of the outstanding equity capital of MeiraGTx UK (the "Reorganization Transaction").

As used in this Agreement:

"Applicable Time" means [•] P.M., New York City time, on June [•], 2018 or such other time as agreed by the Company and the Representatives.

"General Disclosure Package" means any Issuer General Use Free Writing Prospectuses issued at or prior to the Applicable Time, the most recent preliminary prospectus that is distributed to investors prior to the Applicable Time and the information included on Schedule B-1 hereto, all considered together.

"Issuer Free Writing Prospectus" means any "issuer free writing prospectus," as defined in Rule 433 of the 1933 Act Regulations ("Rule 433"), including without limitation any "free writing prospectus" (as defined in Rule 405 of the 1933 Act Regulations ("Rule 405")) relating to the Securities that is (i) required to be filed with the Commission by the Company, (ii) a "road show that is a written communication" within the meaning of Rule 433(d)(8)(i), whether or not required to be filed with the Commission, or (iii) exempt from filing with the Commission pursuant to Rule 433(d)(5)(i) because it contains a description of the Securities or of the offering that does not reflect the final terms, in each case in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company's records pursuant to Rule 433(g).

"Issuer General Use Free Writing Prospectus" means any Issuer Free Writing Prospectus that is intended for general distribution to prospective investors (other than a "*bona fide* electronic road show," as defined in Rule 433 (the "Bona Fide Electronic Road Show")), as evidenced by its being specified in Schedule B-2 hereto.

"Issuer Limited Use Free Writing Prospectus" means any Issuer Free Writing Prospectus that is not an Issuer General Use Free Writing Prospectus.

"Testing-the-Waters Communication" means any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the 1933 Act.

"Written Testing-the-Waters Communication" means any Testing-the-Waters Communication that is a written communication within the meaning of Rule 405 under the 1933 Act.

SECTION 1. Representations and Warranties.

(a) *Representations and Warranties by the Company*. For purposes of construction in this Section 1, MeiraGTx UK and its subsidiaries shall be deemed to be subsidiaries of the Company as of the date hereof and at all times prior to the date hereof. In this Section 1, references to the Company's knowledge, belief or awareness shall mean the knowledge, belief or awareness of each of the Company and MeiraGTx UK. Each of the Company and MeiraGTx UK represent, warrant and covenant, jointly and severally, to each Underwriter, as of the date hereof, the Applicable Time, the Closing Time (as defined below) and any Date of Delivery (as defined below), and agrees with each Underwriter, as follows:

(i) Registration Statement and Prospectuses. Each of the Registration Statement and any amendment thereto has become effective under the 1933 Act. No stop order suspending the effectiveness of the Registration Statement or any post-effective amendment thereto has been issued under the 1933 Act, no order preventing or suspending the use of any preliminary prospectus or the Prospectus has been issued and no proceedings for any of those purposes have been instituted or are pending or, to the Company's knowledge, contemplated. The Company has complied with each request (if any) from the Commission for additional information.

Each of the Registration Statement and any post-effective amendment thereto, at the time it became effective, the Applicable Time, the Closing Time and any Date of Delivery complied and will comply in all material respects with the requirements of the 1933 Act and the 1933 Act Regulations. Each preliminary prospectus, the Prospectus and any amendment or supplement thereto, at the time each was filed with the Commission, and, in each case, at the Applicable Time, the Closing Time and any Date of Delivery complied and will comply in all material respects with the requirements of the 1933 Act and the 1933 Act Regulations. Each preliminary prospectus delivered to the Underwriters for use in connection with this offering and the Prospectus was or will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

(ii) Accurate Disclosure. Neither the Registration Statement nor any amendment thereto, at its effective time, at the Closing Time or at any Date of Delivery, contained, contains or will contain an untrue statement of a material fact or omitted, omits or will omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading. At the Applicable Time and any Date of Delivery, none of (A) the General Disclosure Package, (B) any individual Issuer Limited Use Free Writing Prospectus, when considered together with the General Disclosure Package and (C) any individual Written Testing-the-Waters Communication, when considered together with the General Disclosure Package, included, includes or will include an untrue statement of a material fact or omitted, omits or will omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. Neither the Prospectus nor any amendment or supplement thereto, as of its issue date, at the time of any filing with the Commission pursuant to Rule 424(b), at the Closing Time or at any Date of Delivery, included, includes or will include an untrue statement of a material fact or omitted, omits or will omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading.

The representations and warranties in this subsection shall not apply to statements in or omissions from the Registration Statement (or any amendment thereto), the General Disclosure Package or the Prospectus (or any amendment or supplement thereto) made in reliance upon and in conformity with written information furnished to the Company by any Underwriter through the Representatives expressly for use therein. For purposes of this Agreement, the only information so furnished shall be [the information in the first two sentences of the first paragraph under the heading "Underwriting–Commissions and Discounts," the information in the second, third and fourth paragraphs under the heading "Underwriting–Price Stabilization, Short Positions and Penalty Bids" and the information under the heading "Underwriting–Electronic Offer, Sale and Distribution of Shares"] in each case contained in the Prospectus (collectively, the "Underwriter Information").

(iii) Issuer Free Writing Prospectuses. No Issuer Free Writing Prospectus conflicts or will conflict with the information contained in the Registration Statement or the Prospectus, and any preliminary or other prospectus deemed to be a part thereof that has not been superseded or modified. The Company and MeiraGTx UK has made available a Bona Fide Electronic Road Show in compliance with Rule 433(d)(8)(ii) such that no filing of any "road show" (as defined in Rule 433(h)) is required in connection with the offering of the Securities.

(iv) Testing-the-Waters Materials. Neither the Company nor MeiraGTx UK (A) has alone engaged in any Testing-the-Waters Communication other than Testing-the-Waters Communications with the consent of the Representatives with entities that are qualified institutional buyers within the meaning of Rule 144A under the 1933 Act or institutions that are accredited investors within the meaning of Rule 501 under the 1933 Act and (B) has authorized anyone other than the Representatives to engage in Testing-the-Waters Communications. The Company reconfirms that the Representatives have been authorized to act on its behalf in undertaking Testing-the-Waters Communications. Neither the Company nor MeiraGTx UK has distributed any Written Testing-the-Waters Communications other than those listed on Schedule B hereto.

(v) Company Not Ineligible Issuer. At the time of filing the Registration Statement and any post-effective amendment thereto, at the earliest time thereafter that the Company or another offering participant made a *bona fide* offer (within the meaning of Rule 164(h)(2) of the 1933 Act Regulations) of the Securities and at the date hereof, the Company was not and is not an "ineligible issuer," as defined in Rule 405, without taking account of any determination by the Commission pursuant to Rule 405 that it is not necessary that the Company be considered an ineligible issuer.

(vi) Emerging Growth Company Status. From the time of the initial confidential submission of the Registration Statement to the Commission (or, if earlier, the first date on which the Company engaged directly or through any Person authorized to act on its behalf in any Testing-the-Waters Communication) through the date hereof, the Company has been and is an "emerging growth company," as defined in Section 2(a) of the 1933 Act (an "Emerging Growth Company").

(vii) Independent Accountants. The accountants who certified the financial statements and supporting schedules included in the Registration Statement, the General Disclosure Package and the Prospectus are independent public accountants as required by the 1933 Act, the 1933 Act Regulations and the Public Company Accounting Oversight Board.

(viii) Financial Statements. The financial statements included in the Registration Statement, the General Disclosure Package and the Prospectus, together with the related schedules and notes, present fairly, in all material respects, the financial position of MeiraGTx UK and its consolidated subsidiaries at the dates indicated and the statement of operations, shareholders' equity and cash flows of MeiraGTx UK and its consolidated subsidiaries for the periods specified; said financial statements have been prepared in conformity with U.S. generally accepted accounting principles ("GAAP") applied on a consistent basis throughout the periods involved. The supporting schedules, if any, present fairly, in all material respects, in accordance with GAAP the information required to be stated therein. The selected financial data and the summary financial information included in the Registration Statement, the General Disclosure Package and the Prospectus present fairly, in all material respects, the information shown therein and have been compiled on a basis consistent with that of the audited financial statements included therein. Except as included therein, no historical or pro forma financial statements or supporting schedules are required to be included or incorporated by reference in the Registration Statement, the General Disclosure Package or the Prospectus under the 1933 Act or the 1933 Act Regulations.

(ix) No Material Adverse Change in Business. Except as otherwise stated therein, since the respective dates as of which information is given in the Registration Statement, the General Disclosure Package or the Prospectus, (A) there has been no material adverse change in the condition, financial or otherwise, or in the earnings, business affairs or business prospects of the Company and its subsidiaries considered as one enterprise, whether or not arising in the ordinary course of business (a "Material Adverse Effect"), (B) there have been no transactions entered into by the Company or any of its subsidiaries, other than those in the ordinary course of business, which are material with respect to the Company and its subsidiaries considered as one enterprise, and (C) there has been no dividend or distribution of any kind declared, paid or made by the Company on any class of its shares.

(x) Good Standing of the Company. The Company has been duly incorporated and is validly existing as an exempted company in good standing under the laws of the Cayman Islands and has corporate power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement, the General Disclosure Package and the Prospectus and to enter into and perform its obligations under this Agreement; and the Company is duly qualified as a foreign corporation to transact business and is in good standing in each other jurisdiction in which such qualification is required, whether by reason of the ownership or leasing of property or the conduct of business, except where the failure so to qualify or to be in good standing would not reasonably be expected to result in a Material Adverse Effect.

(xi) Good Standing of Subsidiaries. Each "significant subsidiary" of the Company (as such term is defined in Rule 1-02 of Regulation S-X) (each, a "Subsidiary" and, collectively, the "Subsidiaries") has been duly incorporated or organized and is validly existing in good standing under the laws of the jurisdiction of its incorporation or organization, has corporate or similar power and authority to own, lease and operate its properties and to conduct its business as described in the Registration Statement, the General Disclosure Package and the Prospectus and is duly qualified to transact business and is in good standing in each jurisdiction in which such qualification is required, whether by reason of the ownership or leasing of property or the conduct of business, except where the failure to so qualify or to be in good standing would not result in a Material Adverse Effect. Except as otherwise disclosed in the Registration Statement, the General Disclosure Package and the Prospectus, all of the issued and outstanding capital stock or other equity interests of each Subsidiary has been duly authorized and validly issued, is fully paid and non-assessable and immediately after the Reorganization Transaction, will be owned by the Company, directly or through subsidiaries, free and clear of any security interest, mortgage, pledge, lien, encumbrance, claim or equity. None of the outstanding shares of any Subsidiary were issued in violation of the preemptive or similar rights of any securityholder of such Subsidiary. Immediately after the Reorganization Transaction, the only subsidiaries of the Company will be (A) the subsidiaries listed on Exhibit 21 to the Registration Statement and (B) certain other subsidiaries which, considered in the aggregate as a single subsidiary, do not constitute a "significant subsidiary" as defined in Rule 1-02 of Regulation S-X.

(xii) Capitalization. The authorized, issued and outstanding shares of MeiraGTx UK are as set forth in the Registration Statement, the General Disclosure Package and the Prospectus in the column entitled "Actual" under the caption "Capitalization" (except for subsequent issuances, if any, pursuant to this Agreement, pursuant to reservations, agreements or employee benefit plans referred to in the Registration Statement, the General Disclosure Package and the Prospectus or pursuant to the exercise of convertible securities or options referred to in the Registration Statement, the General Disclosure Package and the Prospectus. The outstanding shares of the Company have been duly authorized and validly issued and are fully paid and non-assessable. None of the outstanding shares of the Company were issued in violation of the preemptive or other similar rights of any securityholder of the Company.

(xiii) Authorization of Agreement. This Agreement has been duly authorized, executed and delivered by the Company and MeiraGTx UK.

(xiv) Authorization and Description of Securities. The Securities to be purchased by the Underwriters from the Company have been duly authorized by resolution of the directors of the Company for issuance and sale to the Underwriters pursuant to this Agreement and, when issued and delivered by the Company pursuant to this Agreement following the Reorganization Transaction against payment of the consideration set forth herein, will be validly issued and fully paid and non-assessable; and the issuance of the Securities is not subject to the preemptive or other similar rights of any securityholder of the Company. The Ordinary Shares conform in all material respects to all statements relating thereto contained in the Registration Statement, the General Disclosure Package and the Prospectus and such description conforms in all material respects to the rights set forth in the instruments defining the same. No holder of Securities will be subject to personal liability by reason of being such a holder.

(xv) Registration Rights. There are no persons with registration rights or other similar rights to have any securities registered for sale pursuant to the Registration Statement or otherwise registered for sale or sold by the Company or MeiraGTx UK under the 1933 Act pursuant to this Agreement.

(xvi) Absence of Violations, Defaults and Conflicts. Neither the Company nor any of its Subsidiaries is (A) in violation of its charter, by-laws or similar organizational document, (B) in default in the performance or observance of any obligation, agreement, covenant or condition contained in any contract, indenture, mortgage, deed of trust, loan or credit agreement, note, lease or other agreement or instrument to which the Company or any of its subsidiaries is a party or by which it or any of them may be bound or to which any of the properties or assets of the Company or any subsidiary is subject (collectively, "Agreements and Instruments"), except for such defaults that would not, reasonably be expected to, singly or in the aggregate, result in a Material Adverse Effect, or (C) in violation of any law, statute, rule, regulation, judgment, order, writ or decree of any arbitrator, court, governmental body, regulatory body, administrative agency or other authority, body or agency having jurisdiction over the Company or any of its subsidiaries or any of their respective properties, assets or operations (each, a "Governmental Entity"), except for such violations that would not reasonably be expected to, singly or in the aggregate, result in a Material

Adverse Effect. The execution, delivery and performance of this Agreement and the consummation of the transactions contemplated herein and in the Registration Statement, the General Disclosure Package and the Prospectus (including the issuance and sale of the Securities and the use of the proceeds from the sale of the Securities as described therein under the caption "Use of Proceeds") and compliance by the Company and MeiraGTx UK with its respective obligations hereunder have been duly authorized by all necessary corporate action and do not and will not, whether with or without the giving of notice or passage of time or both, conflict with or constitute a breach of, or default or Repayment Event (as defined below) under, or result in the creation or imposition of any lien, charge or encumbrance upon any properties or assets of the Company, MeiraGTx UK or any subsidiary pursuant to, the Agreements and Instruments (except for such conflicts, breaches, defaults or Repayment Events or liens, charges or encumbrances that would not, singly or in the aggregate, result in a Material Adverse Effect), nor will such action result in any violation of the provisions of the charter, by-laws or similar organizational document of the Company, MeiraGTx UK or any of its respective subsidiaries or any law, statute, rule, regulation, judgment, order, writ or decree of any Governmental Entity. As used herein, a "Repayment Event" means any event or condition which gives the holder of any note, debenture or other evidence of indebtedness (or any person acting on such holder's behalf) the right to require the repurchase, redemption or repayment of all or a portion of such indebtedness by the Company, MeiraGTx UK or any of its respective subsidiaries.

(xvii) Absence of Labor Dispute. Except as would not reasonably be expected to result in a Material Adverse Effect, no labor dispute with the employees of the Company or any of its subsidiaries exists or, to the knowledge of the Company, is imminent, and to the Company's knowledge, there is no existing or imminent labor disturbance by the employees of any of its or any subsidiary's principal suppliers, manufacturers, customers or contractors.

(xviii) Absence of Proceedings. Except as disclosed in the Registration Statement, the General Disclosure Package and the Prospectus, there is no action, suit, proceeding, inquiry or investigation before or brought by any Governmental Entity now pending or, to the knowledge of the Company, threatened, against or affecting the Company or any of its subsidiaries, which would reasonably be expected to, singly or in the aggregate, result in a Material Adverse Effect, or which would reasonably be expected to singly or in the aggregate, materially and adversely affect their respective properties or assets or the consummation of the transactions contemplated in this Agreement or the performance by the Company of its obligations hereunder; and the aggregate of all pending legal or governmental proceedings to which the Company or any such subsidiary is a party or of which any of their respective properties or assets is the subject which are not described in the Registration Statement, the General Disclosure Package and the Prospectus, including ordinary routine litigation incidental to the business, would not reasonably be expected to, singly or in the aggregate, result in a Material Adverse Effect.

(xix) Accuracy of Exhibits. There are no contracts or documents which are required to be described in the Registration Statement, the General Disclosure Package or the Prospectus or to be filed as exhibits to the Registration Statement which have not been so described and filed as required.

(xx) Absence of Further Requirements. No filing with, or authorization, approval, consent, license, order, registration, qualification or decree of, any Governmental Entity is necessary or required for the performance by the Company and MeiraGTx UK of its respective obligations hereunder, in connection with the offering, issuance or sale of the Securities hereunder or the consummation of the transactions contemplated by this Agreement, except as have been already obtained or as may be required under the 1933 Act, the 1933 Act Regulations, the rules of the Nasdaq Global Market, state securities laws or the rules of the Financial Industry Regulatory Authority, Inc. ("FINRA").

(xxi) Possession of Licenses and Permits. The Company and its subsidiaries possess such permits, licenses, approvals, consents and other authorizations (collectively, "Governmental Licenses") issued by the appropriate Governmental Entities necessary to conduct the business now operated by them, except where the failure so to possess would not, singly or in the aggregate, result in a Material Adverse Effect. The Company and its subsidiaries are in compliance with the terms and conditions of all Governmental Licenses, except where the failure so to comply would not reasonably be expected to, singly or in the aggregate, result in a Material Adverse Effect. All of the Governmental Licenses are valid and in full force and effect, except when the invalidity of such Governmental Licenses or the failure of such Governmental Licenses to be in full force and effect would not reasonably be expected to, singly or in the aggregate, result in a Material Adverse Effect. Neither the Company nor any of its subsidiaries has received any notice of proceedings relating to the revocation or modification of any Governmental Licenses which, singly or in the aggregate, if the subject of an unfavorable decision, ruling or finding, would result in a Material Adverse Effect.

(xxii) Title to Property. The Company and its subsidiaries have good and marketable title to all real property owned by them and good title to all other properties owned by them, in each case, free and clear of all mortgages, pledges, liens, security interests, claims, restrictions or encumbrances of any kind except such as (A) are described in the Registration Statement, the General Disclosure Package and the Prospectus or (B) do not, singly or in the aggregate, materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company or any of its subsidiaries; and all of the leases and subleases material to the business of the Company and its subsidiaries, considered as one enterprise, and under which the Company or any of its subsidiaries holds properties described in the Registration Statement, the General Disclosure Package or the Prospectus, are in full force and effect, and neither the Company nor any such subsidiary has any notice of any material claim of any sort that has been asserted by anyone adverse to the rights of the Company or any subsidiary under any of the leases or subleases mentioned above, or affecting or questioning the rights of the Company or such subsidiary to the continued possession of the leased or subleased premises under any such lease or sublease.

(xxiii) Possession of Intellectual Property. The Company and its subsidiaries own or possess, or can acquire on reasonable terms, adequate patents, patent rights, licenses, inventions, copyrights, know-how (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures), trademarks, service marks, trade names or other intellectual property necessary to carry on the business as now operated by them, and as proposed to be operated in the future, as disclosed in the Registration Statement, the General Disclosure Package and the Prospectus (collectively, "Intellectual Property"). To the Company's knowledge, except as disclosed in the Registration Statement, the General Disclosure Package and the Prospectus, the conduct of the Company and its subsidiaries' respective businesses does not and will not infringe any issued patents or misappropriate any trade secrets of third parties. The Intellectual Property of the Company has not been adjudged by a court of competent jurisdiction to be invalid or unenforceable, in whole or in part, and the Company is unaware of any facts which would form a reasonable basis for any such adjudication. Neither the Company nor any of its subsidiaries has received any notice of any claim, or is otherwise aware, of any patent infringement or trade secret misappropriation. Neither the Company nor any of its subsidiaries has received any notice of any claim, or is otherwise aware, of any facts or circumstances which would render any Intellectual Property of the Company invalid or inadequate to protect the interest of the Company or any of its subsidiaries therein. To the Company's knowledge: (i) there are no third parties who have rights to any Intellectual Property, except for customary reversionary rights of third-party licensors with respect to Intellectual Property that is disclosed in the Registration Statement, the General Disclosure Package or the Prospectus as owned by or licensed to the Company or its subsidiaries; and (ii) there is no infringement by third parties of any Intellectual Property. There is no pending or, to the Company's knowledge, threatened action, suit, proceeding or claim by others: challenging the Company's rights in or to any Intellectual Property of the Company, and the Company is unaware of any facts which would form a reasonable basis for any such action, suit, proceeding or claim. Except as would not reasonably be expected, individually or in the aggregate, to have a material Adverse Effect, the Company and its subsidiaries have complied with the terms of each agreement pursuant to which Intellectual Property has been licensed to the Company or its subsidiaries, and all such agreements are in full force and effect. To the Company's knowledge, there are no material defects in any of the patents or patent applications included in the Intellectual Property. The Company and its subsidiaries have taken all reasonable steps to protect, maintain and safeguard their Intellectual Property, including the execution of appropriate nondisclosure, confidentiality agreements and invention assignment agreements and invention assignments with their employees, and (Y) to the Company's knowledge, no employee of the Company is in or has been in violation of any term of any employment contract, patent disclosure agreement, invention assignment agreement, non-competition agreement, non-solicitation agreement, nondisclosure agreement, or any restrictive covenant to or with a former employer where the basis of such violation relates to such employee's employment with the Company. The duty of candor and good faith as required by the United States Patent and Trademark Office during the prosecution of the United States patents and patent applications included in the Intellectual Property have been complied with; and in all foreign offices having similar requirements, all such requirements have been complied with. To the Company's knowledge, none of the Company owned Intellectual Property or technology (including information technology and outsourced arrangements) employed by the Company or its subsidiaries has been obtained or is being used by the Company or its subsidiary in violation of any contractual obligation binding on the Company or its subsidiaries or any of their respective officers, directors or employees or otherwise in violation of the rights of any persons. The product candidates described in the Registration Statement, the General Disclosure Package or the Prospectus as under development by the Company or its subsidiaries fall within the scope of the claims of one or more patents or patent applications owned by, or exclusively licensed to, the Company or its subsidiaries.

(xxiv) Environmental Laws. Except as described in the Registration Statement, the General Disclosure Package and the Prospectus or would not, singly or in the aggregate, result in a Material Adverse Effect, (A) neither the Company nor any of its subsidiaries is in violation of any federal, state, local or foreign statute, law, rule, regulation, ordinance, code, policy or rule of common law or any judicial or administrative interpretation thereof, including any judicial or administrative order, consent, decree or judgment, relating to pollution or protection of human health, the environment (including, without limitation, ambient air, surface water, groundwater, land surface or subsurface strata) or wildlife, including, without limitation, laws and regulations relating to the release or threatened release of chemicals, pollutants, contaminants, wastes, toxic substances, hazardous substances, petroleum or petroleum products, asbestos-containing materials or mold (collectively, "Hazardous Materials") or to the manufacture, processing, distribution, use, treatment, storage, disposal, transport or handling of Hazardous Materials (collectively, "Environmental Laws"), (B) the Company and its subsidiaries have all permits, authorizations and approvals required under any applicable Environmental Laws and are each in compliance with their requirements, (C) there are no pending or, to the knowledge of the Company, threatened administrative, regulatory or judicial actions, suits, demands, demand letters, claims, liens, notices of noncompliance or violation, investigations or proceedings relating to any Environmental Law against the Company or any of its subsidiaries and (D) to the knowledge of the Company, there are no events or circumstances that would reasonably be expected to form the basis of an order for clean-up or remediation, or an action, suit or proceeding by any private party or Governmental Entity, against or affecting the Company or any of its subsidiaries relating to Hazardous Materials or any Environmental Laws.

(xxv) Accounting Controls. The Company and each of its subsidiaries maintain effective internal control over financial reporting (as defined under Rule 13-a15 and 15d-15 under the 1934 Act Regulations) and a system of internal accounting controls sufficient to provide reasonable assurances that (A) transactions are executed in accordance with management's general or specific authorization; (B) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain accountability for assets; (C) access to assets is permitted only in accordance with management's general or specific authorization; and (D) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. Except as described in the Registration Statement, the General Disclosure Package and the Prospectus, since the end of the Company's most recent audited fiscal year, there has been (1) no material weakness in the Company's internal control over financial reporting (whether or not remediated) and (2) no change in the Company's internal control over financial reporting that has materially and adversely affected, or is reasonably likely to materially and adversely affect, the Company's internal control over financial reporting.

(xxvi) Compliance with the Sarbanes-Oxley Act. The Company has taken all necessary actions to ensure that, upon the effectiveness of the Registration Statement, it will be in compliance in all material respects with all provisions of the Sarbanes-Oxley Act of 2002 and all rules and regulations promulgated thereunder or implementing the provisions thereof (the "Sarbanes-Oxley Act") that are then in effect and with which the Company is required to comply as of the effectiveness of the Registration Statement, and is taking reasonable steps to enable it to be in compliance with other provisions of the Sarbanes-Oxley Act not currently in effect, upon the effectiveness of such provisions, or which will become applicable to the Company at all times after the effectiveness of the Registration Statement.

(xxvii) Payment of Taxes. All United States federal and U.K. income and other material tax returns of the Company and its subsidiaries required by law to be filed have been filed and all taxes shown by such returns or otherwise assessed, which are due and payable, have been paid, except assessments against which appeals have been taken and as to which adequate reserves have been provided. The Company and its subsidiaries have filed all other tax returns that are required to have been filed by them pursuant to applicable foreign, state, local or other law except insofar as the failure to file such returns would not result in a Material Adverse Effect, and has paid all taxes due pursuant to such returns or pursuant to any assessment received by the Company and its subsidiaries, except for such taxes, if any, as are being contested in good faith and as to which adequate reserves have been established by the Company. The charges, accruals and reserves on the books of the Company in respect of any income and corporation tax liability for any years not finally determined are adequate to meet any assessments or re-assessments for additional income tax for any years not finally determined, except to the extent of any inadequacy that would not result in a Material Adverse Effect.

(xxviii) No Stamp or Transfer Taxes. Except as disclosed in the Registration Statement, the General Disclosure Package and Prospectus, no documentary, registration, transfer, stamp or other similar taxes or duties including, for the avoidance of doubt, UK stamp duty and UK stamp duty reserve tax ("Transfer Taxes") are payable by or on behalf of the Underwriters, the Company or any of its subsidiaries in the United Kingdom or to any taxing authority thereof or therein in connection with (i) the execution, delivery or consummation of this Agreement, (ii) the creation, allotment and issuance of the Securities, (iii) the initial sale and delivery of the Securities to the Underwriters or purchasers procured by the Underwriters in the manner contemplated herein, or (iv) the resale and delivery of the Securities by the Underwriters in the manner contemplated herein.

(xxix) Insurance. The Company and its subsidiaries carry or are entitled to the benefits of insurance, with financially sound and reputable insurers, in such amounts and covering such risks as is generally maintained by similarly sized companies of established repute engaged in the same or similar business, and all such insurance is in full force and effect. The Company has no reason to believe that it or any of its subsidiaries will not be able (A) to renew its existing insurance coverage as and when such policies expire or (B) to obtain comparable coverage from similar institutions as may be necessary or appropriate to conduct its business as now conducted and at a cost that would not result in a Material Adverse Effect. Neither of the Company nor any of its subsidiaries has been denied any insurance coverage which it has sought or for which it has applied.

(xxx) Investment Company Act. Each of the Company and MeiraGTx UK is not required, and upon the issuance and sale of the Securities as herein contemplated and the application of the net proceeds therefrom as described in the Registration Statement, the General Disclosure Package and the Prospectus will not be required, to register as an “investment company” under the Investment Company Act of 1940, as amended (the “1940 Act”).

(xxxi) Absence of Manipulation. Each of the Company and MeiraGTx UK has not taken, directly or indirectly, in relation to the offering of the Securities or otherwise, any action or engaged in any course of conduct in breach of, and has taken adequate measures and has adequate procedures in place in order to ensure compliance with, and none of the issue of the Securities, the sale of the Securities and the consummation of the transactions contemplated by this Agreement will constitute a violation by the Company or MeiraGTx UK of, any applicable U.K., US or any other relevant jurisdiction “insider dealing,” “insider trading” or similar legislation and, so far as the Company is aware, no person acting on its behalf has breached or is in breach of any relevant market abuse or insider trading law or regulation, including any reporting obligations to the Commission or any other authority. None of the Company, MeiraGTx UK nor any affiliate of the Company or MeiraGTx UK has taken, nor will the Company, MeiraGTx UK or any affiliate of the Company or MeiraGTx UK take, directly or indirectly, any action which is designed, or would be expected, to cause or result in, or which constitutes, the stabilization or manipulation of the price of any security of the Company or MeiraGTx UK to facilitate the sale or resale of the Securities or to result in a violation of Regulation M under the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder (collectively, the “1934 Act”).

(xxxii) Foreign Corrupt Practices Act. None of the Company, any of its subsidiaries or, to the knowledge of the Company, any director, officer, agent, employee, affiliate or other person acting on behalf of the Company or any of its subsidiaries is aware of or has taken any action, directly or indirectly, that would result in a violation by such persons of the Foreign Corrupt Practices Act of 1977, as amended, and the rules and regulations thereunder (the “FCPA”), including, without limitation, making use of the mails or any means or instrumentality of interstate commerce corruptly in furtherance of an offer, payment, promise to pay or authorization of the payment of any money, or other property, gift, promise to give, or authorization of the giving of anything of value to any “foreign official” (as such term is defined in the FCPA) or any foreign political party or official thereof or any candidate for foreign political office, in contravention of the FCPA and the Company and, to the knowledge of the Company, its affiliates have conducted their businesses in compliance with the FCPA and have instituted and maintain policies and procedures designed to ensure, and which are reasonably expected to continue to ensure, continued compliance therewith.

(xxxiii) Money Laundering Laws. The operations of the Company and its subsidiaries are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the money laundering statutes of all applicable jurisdictions, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any Governmental Entity (collectively, the "Money Laundering Laws"); and no action, suit or proceeding by or before any Governmental Entity involving the Company or any of its subsidiaries with respect to the Money Laundering Laws is pending or, to the best knowledge of the Company, threatened.

(xxxiv) OFAC. None of the Company, any of its subsidiaries or, to the knowledge of the Company, any director, officer, agent, employee, affiliate or representative of the Company or any of its subsidiaries is an individual or entity ("Person") currently the subject or target of any sanctions administered or enforced by the United States Government, including, without limitation, the U.S. Department of the Treasury's Office of Foreign Assets Control ("OFAC"), the United Nations Security Council ("UNSC"), the European Union, Her Majesty's Treasury ("HMT"), or other relevant sanctions authority (collectively, "Sanctions"), nor is the Company located, organized or resident in a country or territory that is the subject of Sanctions; and the Company will not directly or indirectly use the proceeds of the sale of the Securities, or lend, contribute or otherwise make available such proceeds to any subsidiaries, joint venture partners or other Person, to fund any activities of or business with any Person, or in any country or territory, that, at the time of such funding, is the subject of Sanctions or in any other manner that will result in a violation by any Person (including any Person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions.

(xxxv) [Reserved].

(xxxvi) Lending Relationship. Except as disclosed in the Registration Statement, the General Disclosure Package and the Prospectus, the Company and MeiraGTx UK (i) does not have any material lending or other relationship with any bank or lending affiliate of any Underwriter and (ii) does not intend to use any of the proceeds from the sale of the Securities to repay any outstanding debt owed to any affiliate of any Underwriter.

(xxxvii) Statistical and Market-Related Data. Any statistical and market-related data included in the Registration Statement, the General Disclosure Package or the Prospectus are based on or derived from sources that the Company believes, after reasonable inquiry, to be reliable and accurate in all material respects and, to the extent required, the Company has obtained the written consent to the use of such data from such sources.

(xxxviii) Regulatory Matters. Except as described in the Registration Statement, the General Disclosure Package and the Prospectus, and except as would not, individually or in the aggregate, have or may reasonably be expected to have a Material Adverse Effect: (i) neither the Company nor any of its subsidiaries has received any written notice of adverse filing, warning letter, untitled letter or other correspondence or notice from the U.S. Food and Drug Administration or other Governmental Entity, alleging or asserting material noncompliance with the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 301 et seq.) (the "FFDCA"), section 351 of the Public Health Service Act (42 U.S.C. § 262) ("section 351 of the PHSA") or similar state, federal or foreign law or regulation; (ii) the Company and any subsidiary, and to the Company's knowledge, their respective directors, officers, employees or agents, are and have been in compliance in all material respects with all applicable health care laws, including without limitation, (A) the FFDCA and PHSA; (B) all applicable federal, state, local and all applicable foreign healthcare related fraud and abuse laws, including, without limitation, the federal Anti-kickback Statute (42 U.S.C. § 1320a-7b(b)), the civil False Claims Act (31 U.S.C. §§ 3729 et seq.), the criminal False Claims Law (42 U.S.C. § 1320a-7b(a)), all criminal laws relating to health care fraud and abuse, including, but not limited to, 18 U.S.C. §§ 286 and 287, the health care fraud criminal provisions under the U.S. Health Insurance Portability and Accountability Act of 1996 ("HIPAA") (42 U.S.C. §§ 1320d et seq.), the exclusion law (42 U.S.C. § 1320a-7), the civil monetary penalties law (42 U.S.C. § 1320a-7a) and the U.S. Physician Payments Sunshine Act (42 U.S.C. § 1320a-7h); (C) Medicare (Title XVIII of the Social Security Act); (D) Medicaid (Title XIX of the Social Security Act); (E) HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (42 U.S.C. §§ 17921 et seq.); (F) the regulations promulgated pursuant to such laws; and (G) any other similar local, state, federal, or foreign laws (collectively, "Health Care Laws"); (iii) neither the Company nor any subsidiary has received written notice of any ongoing claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any U.S. or non-U.S. Governmental Entity or third party alleging that any product operation or activity is in violation of any Health Care Law or has any knowledge that any such Governmental Entity or third party is considering any such claim, litigation, arbitration, action, suit, investigation or proceeding; (iv) neither the Company nor any subsidiary has received written notice that any Governmental Entity has taken, is taking or intends to take action to limit, suspend, modify or revoke any applicable Governmental Licenses or has any knowledge that any such Governmental Entity is considering such action; (v) the Company and each subsidiary has filed, obtained, maintained or submitted all material reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by all Health Care Laws and that all such material reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete, correct and not misleading on the date filed (or were corrected or supplemented by a subsequent submission); (vi) neither the Company nor any subsidiary or any of their respective directors, officers, employees or, to the Company's knowledge, or agents is or has been debarred, suspended or excluded, or has been convicted of any crime or engaged in any conduct that would result in a debarment, suspension or exclusion from any federal or state government health care program; and (vii) the Company is not a party to, and does not have any ongoing reporting obligations pursuant to any corporate integrity agreement, deferred prosecution agreement, monitoring agreement, consent decree, settlement order, plan of correction or similar agreement imposed by any Government Entity.

(xxxix) Preclinical and Clinical Studies. The preclinical and clinical studies conducted by or on behalf of the Company have been and, if still pending, are being conducted in accordance with experimental protocols, procedures and controls pursuant to all applicable Health Care Laws and Governmental Licenses; the descriptions of the results of such preclinical and clinical studies contained in the Registration Statement, the General Disclosure Package and the Prospectus are accurate and complete in all material respects and fairly present the data derived from such preclinical and clinical studies; except to the extent disclosed in the Registration Statement, the General Disclosure Package and the Prospectus, the Company is not aware of any preclinical or clinical studies, the results of which the Company believes reasonably call into question the preclinical or clinical study results described in the Registration Statement, the General Disclosure Package and the Prospectus when viewed in the context in which such results are described; and neither the Company nor any of its Subsidiaries has received any notices or correspondence from any Governmental Authority requiring the termination or suspension, or except as disclosed in the Registration Statement, General Disclosure Packages and Prospectus, any modification of any preclinical or clinical study conducted by or on behalf of the Company, except as described in the Registration Statement, the General Disclosure Package and the Prospectus or as would not, individually or in the aggregate, have or reasonably be expected to have a Material Adverse Effect.

(xl) Cybersecurity. (i)(x) To the Company's knowledge, there has been no material security breach or attack or other compromise of or relating to any of the Company's and its subsidiaries' information technology and computer systems, networks, hardware, software, data (including the data of their respective employees, suppliers, vendors and any third party data maintained by or on behalf of them), equipment or technology ("IT Systems and Data") and (y) the Company and its subsidiaries have not been notified of, and have no knowledge of any event or condition that would reasonably be expected to result in, any security breach, attack or compromise to their IT Systems and Data, (ii) the Company and its subsidiaries have complied, and are presently in compliance, with, all applicable laws, statutes or any applicable judgment, order, rule or regulation of any court or arbitrator or governmental or regulatory authority and all applicable industry guidelines, standards, internal policies and contractual obligations relating to the privacy and security of IT Systems and Data and to the protection of such IT Systems and Data from unauthorized use, access, misappropriation or modification, except in the case of this clause (ii), individually or in the aggregate, would not reasonably be expected to have a Material Adverse Effect and (iii) the Company and its subsidiaries have implemented backup and disaster recovery technology consistent with industry standards and practices.

(xli) Passive Foreign Investment Company. Subject to the qualifications, limitations, exceptions and assumptions set forth in the Registration Statement, General Disclosure Packages and the Prospectus, the Company believes that it was not a passive foreign investment company ("PFIC") within the meaning of Section 1297 of the Internal Revenue Code of 1986, as amended, for its most recently completed taxable year and it does not expect to be a PFIC for its current taxable year.

(xlii) Proper Form. This Agreement is in proper form to be enforceable in the Cayman Islands in accordance with its terms; to ensure the legality, validity, enforceability or admissibility into evidence in the Cayman Islands of this Agreement it is not necessary that this Agreement be filed or recorded with any court or other authority in the Cayman Islands (other than court filings in the ordinary course of proceedings) or that any stamp or similar tax in the Cayman Islands (other than court fees or similar documentary tax payable in the ordinary course of proceedings) be paid on or in respect of this Agreement or any other documents to be furnished hereunder or thereunder.

(xliii) No Immunity. Neither the Company nor any of its subsidiaries has any right of immunity under New York or United States law or the law of the Cayman Islands, from any legal action, suit or proceeding, from the giving of any relief in any such legal action, suit or proceeding, from set-off or counterclaim, from the jurisdiction of any New York or United States federal court or court in the Cayman Islands, from service of process, attachment upon or prior judgment, or attachment in aid of execution of judgment, or from execution of a judgment, or other legal process or proceeding for the giving of any relief or for the enforcement of a judgment, in any such court, with respect to its obligations, liabilities or any other matter under or arising out of or in connection with this Agreement. To the extent that the Company or any of its subsidiaries may have or may hereafter become entitled to any such right of immunity in any such court in which proceedings may at any time be commenced, the Company and any such subsidiary waives or will waive such right to the extent permitted by law and has consented to such relief and enforcement as provided in Section 16 of this Agreement.

(xliv) Valid Choice of Law. Each of the Company and MeiraGTx UK has the power to submit, and pursuant to Section 16 of this Agreement, has legally, validly, effectively and irrevocably submitted, to the personal jurisdiction of each United States federal court and New York state court located in the Borough of Manhattan, in the City of New York, New York, U.S.A. (each, a "New York Court"), and each of the Company and MeiraGTx UK has the power to designate, appoint and authorize, and pursuant to Section 16 of this Agreement, has legally, validly, effectively and irrevocably designated, appointed and authorized an agent for service of process in any action arising out of or relating to this Agreement in any New York Court, and service of process effected on such authorized agent will be effective to confer valid personal jurisdiction over each of the Company and MeiraGTx UK as provided in Section 16 hereof.

(xlv) Final Judgments. Any final judgment for a fixed or readily calculable sum of money rendered by a New York Court having jurisdiction under its own domestic laws in respect of any suit, action or proceeding against the Company or MeiraGTx UK based upon this Agreement and any instruments or agreements entered into for the consummation of the transactions contemplated herein would be enforceable against the Company or MeiraGTx UK, as applicable, without re-examination of the merits of the underlying dispute, by an action commenced on the foreign judgment debt in the Grand Court of the Cayman Islands, provided such judgment (A) is given by a foreign court of competent jurisdiction; (B) imposes on the judgment debtor a liability to pay a liquidated sum for which the judgment has been given; (C) is final; (D) is not in respect of taxes, a fine or penalty; and (E) was not obtained in a manner and is not of a kind the enforcement of which is contrary to natural justice or the public policy of the Cayman Islands.

(xlvi) No Rated Securities. Neither the Company nor its subsidiaries have any debt securities or preferred shares that are rated by any "nationally recognized statistical rating agency" (as defined in Section 3(a)(62) of the 1934 Act)."

(xlvii) Certificate Regarding Beneficial Ownership. The Company has provided to the Representatives a properly completed and executed Certification Regarding Beneficial Owners of Legal Entity Customers, together with copies of any required identifying documentation, and the Company hereby undertakes to provide such additional supporting documentation as the Representatives may reasonably request in connection with the verification of the foregoing certification.

(b) *Officer's Certificates*. Any certificate signed by any officer of the Company or any of its subsidiaries delivered to the Representatives or to counsel for the Underwriters shall be deemed a representation and warranty by the Company to each Underwriter as to the matters covered thereby.

SECTION 2. Sale and Delivery to Underwriters; Closing.

(a) *Initial Securities*. On the basis of the representations and warranties herein contained and subject to the terms and conditions herein set forth, the Company agrees to sell to each Underwriter, severally and not jointly, and each Underwriter, severally and not jointly, agrees to subscribe for from the Company, at the price per share set forth in Schedule A, that number of Initial Securities set forth in Schedule A opposite the name of such Underwriter, plus any additional number of Initial Securities which such Underwriter may become obligated to subscribe for pursuant to the provisions of Section 10 hereof, subject, in each case, to such adjustments among the Underwriters as the Representatives in their discretion shall make to eliminate any sales of or subscriptions for fractional shares.

(b) *Option Securities*. In addition, on the basis of the representations and warranties herein contained and subject to the terms and conditions herein set forth, the Company hereby grants an option to the Underwriters, severally and not jointly, to subscribe for up to an additional [•] Ordinary Shares, at the price per share set forth in Schedule A, less an amount per share equal to any dividends or distributions declared by the Company and payable on the Initial Securities but not payable on the Option Securities. The option hereby granted may be exercised for 30 days after the date hereof and may be exercised in whole or in part at any time from time to time upon notice by the Representatives to the Company setting forth the number of Option Securities as to which the several Underwriters are then exercising the option and the time and date of payment and delivery for such Option Securities. Any such time and date of delivery (a "Date of Delivery") shall be determined by the Representatives, but shall not be later than seven full business days after the exercise of said option, nor in any event prior to the Closing Time. If the option is exercised as to all or any portion of the Option Securities, each of the Underwriters, acting severally and not jointly, will subscribe for that proportion of the total number of Option Securities then being subscribed for which the number of Initial Securities set forth in Schedule A opposite the name of such Underwriter bears to the total number of Initial Securities, subject, in each case, to such adjustments as the Representatives in their discretion shall make to eliminate any sales of or subscriptions for fractional shares.

(c) *Payment*. Payment of the subscription price for, and delivery of certificates or security entitlements for, the Initial Securities shall be made at the offices of Cooley LLP, 1114 Avenue of the Americas, New York, NY 10036, or at such other place as shall be agreed upon by the Representatives and the Company, at 9:00 A.M. (New York City time) on the second (third, if the pricing occurs after 4:30 P.M. (New York City time) on any given day) business day after the date hereof (unless postponed in accordance with the provisions of Section 10), or such other time not later than ten business days after such date as shall be agreed upon by the Representatives and the Company (such time and date of payment and delivery being herein called "Closing Time").

In addition, in the event that any or all of the Option Securities are subscribed for by the Underwriters, payment of the subscription price for, and delivery of certificates or security entitlements for, such Option Securities shall be made at the above-mentioned offices, or at such other place as shall be agreed upon by the Representatives and the Company, on each Date of Delivery as specified in the notice from the Representatives to the Company.

Payment shall be made to the Company by wire transfer of immediately available funds to a bank account designated by the Company against delivery to the Representatives for the respective accounts of the Underwriters of certificates or security entitlements for the Securities to be subscribed for by them. It is understood that each Underwriter has authorized the Representatives, for its account, to accept delivery of, receipt for, and make payment of the subscription price for, the Initial Securities and the Option Securities, if any, which it has agreed to subscribe for. Each of Merrill Lynch and Barclays Capital Inc., individually and not as a representative of the Underwriters, may (but shall not be obligated to) make payment of the subscription price for the Initial Securities or the Option Securities, if any, to be subscribed for by any Underwriter whose funds have not been received by the Closing Time or the relevant Date of Delivery, as the case may be, but such payment shall not relieve such Underwriter from its obligations hereunder.

SECTION 3. Covenants of the Company and MeiraGTx UK. Each of the Company and MeiraGTx UK covenants with each Underwriter as follows:

(a) *Compliance with Securities Regulations and Commission Requests*. The Company, subject to Section 3(b), will comply with the requirements of Rule 430A, and will promptly notify the Representatives, and confirm the notice in writing, (i) when any post-effective amendment to the Registration Statement shall become effective or any amendment or supplement to the Prospectus shall have been filed, (ii) of the receipt of any comments from the Commission, (iii) of any request by the Commission for any amendment to the Registration Statement or any amendment or supplement to the Prospectus or for additional information, (iv) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement or any post-effective amendment or of any order preventing or suspending the use of any preliminary prospectus or the Prospectus, or of the suspension of the qualification of the Securities for offering or sale in any jurisdiction, or of the initiation or threatening of any proceedings for any of such purposes or of any examination pursuant to Section 8(d) or 8(e) of the 1933 Act concerning the Registration Statement and (v) if the Company becomes the subject of a proceeding under Section 8A of the 1933 Act in connection with the offering of the Securities. The Company will effect all filings required under Rule 424(b), in the manner and within the time period required by Rule 424(b) (without reliance on Rule 424(b)(8)), and will take such steps as it deems necessary to ascertain promptly whether the form of prospectus transmitted for filing under Rule 424(b) was received for filing by the Commission and, in the event that it was not, it will promptly file such prospectus. The Company will make every reasonable effort to prevent the issuance of any stop order, prevention or suspension and, if any such order is issued, to obtain the lifting thereof as soon as practicable.

(b) *Continued Compliance with Securities Laws*. The Company will comply with the 1933 Act and the 1933 Act Regulations so as to permit the completion of the distribution of the Securities as contemplated in this Agreement and in the Registration Statement, the General Disclosure Package and the Prospectus. If at any time when a prospectus relating to the Securities is (or, but for the exception afforded by Rule 172 of the 1933 Act Regulations ("Rule 172"), would be) required by the 1933 Act to be delivered in connection with sales of the Securities, any event shall occur or condition shall exist as a result of which it is necessary, in the opinion of counsel for the Underwriters or for the Company, to (i) amend the Registration Statement in order that the Registration Statement will not include an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading, (ii) amend or supplement the General Disclosure Package or the Prospectus in order that the General Disclosure Package or the Prospectus, as the case may be, will not include any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein not misleading in the light of the circumstances existing at the time it is delivered to a subscriber or (iii) amend the Registration Statement or amend or supplement the General Disclosure Package or the Prospectus, as the case may be, in order to comply with the requirements of the 1933 Act or the 1933 Act Regulations, the Company will promptly (A) give the Representatives notice of such event, (B) prepare any amendment or supplement as may be necessary to correct such statement or omission or to make the Registration Statement, the General Disclosure Package or the Prospectus comply with such requirements and, a reasonable amount of time prior to any proposed filing or use, furnish the Representatives with copies of any such amendment or supplement and (C) file with the Commission any such amendment or supplement; provided that the Company shall not file or use any such amendment or supplement to which the Representatives or counsel for the Underwriters shall object. The Company will furnish to the Underwriters such number of copies of such amendment or supplement as the Underwriters may reasonably request. The Company has given the Representative(s) notice of any filings made pursuant to the 1934 Act or 1934 Act Regulations within 48 hours prior to the Applicable Time; the Company will give the Representative(s) notice of its intention to make any such filing from the Applicable Time to the Closing Time and will furnish the Representative(s) with copies of any such documents a reasonable amount of time prior to such proposed filing.

(c) *Delivery of Registration Statements*. The Company has furnished or will deliver to the Representatives and counsel for the Underwriters, without charge, signed copies of the Registration Statement as originally filed and each amendment thereto (including exhibits filed therewith) and signed copies of all consents and certificates of experts, and will also deliver to the Representatives, without charge, a conformed copy of the Registration Statement as originally filed and each amendment thereto (without exhibits) for each of the Underwriters. The copies of the Registration Statement and each amendment thereto furnished to the Underwriters will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

(d) *Delivery of Prospectuses*. The Company has delivered to each Underwriter, without charge, as many copies of each preliminary prospectus as such Underwriter reasonably requested, and the Company hereby consents to the use of such copies for purposes permitted by the 1933 Act. The Company will furnish to each Underwriter, without charge, during the period when a prospectus relating to the Securities is (or, but for the exception afforded by Rule 172, would be) required to be delivered under the 1933 Act, such number of copies of the Prospectus (as amended or supplemented) as such Underwriter may reasonably request. The Prospectus and any amendments or supplements thereto furnished to the Underwriters will be identical to the electronically transmitted copies thereof filed with the Commission pursuant to EDGAR, except to the extent permitted by Regulation S-T.

(e) *Blue Sky Qualifications*. The Company will use its reasonable best efforts, in cooperation with the Underwriters, to qualify the Securities for offering and sale under the applicable securities laws of such states and other jurisdictions (domestic or foreign) as the Representatives may designate and to maintain such qualifications in effect so long as required to complete the distribution of the Securities; provided, however, that the Company shall not be obligated to file any general consent to service of process or to qualify as a foreign corporation or as a dealer in securities in any jurisdiction in which it is not so qualified or to subject itself to taxation in respect of doing business in any jurisdiction in which it is not otherwise so subject.

(f) *Rule 158*. The Company will timely file such reports pursuant to the 1934 Act as are necessary in order to make generally available to its securityholders as soon as practicable an earnings statement for the purposes of, and to provide to the Underwriters the benefits contemplated by, the last paragraph of Section 11(a) of the 1933 Act.

(g) *Use of Proceeds*. The Company will use the net proceeds received by it from the sale of the Securities in the manner specified in the Registration Statement, the General Disclosure Package and the Prospectus under "Use of Proceeds."

(h) *Listing*. The Company will use its reasonable best efforts to effect and maintain the listing of the Ordinary Shares (including the Securities) on the Nasdaq Global Market.

(i) *Restriction on Sale of Securities*. During a period of 180 days from the date of the Prospectus, each of the Company and MeiraGTx UK will not, without the prior written consent of the Representatives, (i) directly or indirectly, 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 or otherwise transfer or dispose of any Ordinary Shares or any securities convertible into or exercisable or exchangeable for Ordinary Shares or file or confidentially submit any registration statement under the 1933 Act with respect to any of the foregoing or (ii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the Ordinary Shares, whether any such swap or transaction described in clause (i) or (ii) above is to be settled by delivery of Ordinary Shares or other securities, in cash or otherwise. The foregoing sentence shall not apply to (A) the Securities to be sold hereunder, (B) any Ordinary Shares issued by the Company upon the exercise of an option or warrant or the conversion of a security outstanding on the date hereof and referred to in the Registration Statement, the General Disclosure Package and the Prospectus, (C) any Ordinary Shares issued or options to purchase equity Ordinary Shares or other equity awards covering Ordinary Shares granted pursuant to existing employee benefit plans of the Company referred to in the Registration Statement, the General Disclosure Package and the Prospectus or (D) any Ordinary Shares issued pursuant to any non-employee director compensation plan or program or dividend reinvestment plan referred to in the Registration Statement, the General Disclosure Package and the Prospectus, (E) the filing by the Company of a registration statement with the Commission on Form S-8 in respect of any shares or other equity instruments issued pursuant to any plans or programs described in (C) or (D) above, or (F) the sale or issuance of or entry into an agreement to sell or issue Ordinary Shares or securities convertible into or exercisable or exchangeable for Ordinary Shares in connection with any (1) mergers, (2) acquisition of securities, businesses, property or other assets, (3) joint ventures or (4) strategic alliances or relationships; provided, that the aggregate number of Ordinary Shares or securities convertible into or exercisable for Ordinary Shares (on an as-converted or as-exercised basis, as the case may be) that the Company may sell or issue or agree to sell or issue pursuant to this clause (F) shall not exceed 5% of the total number of the Company's Ordinary Shares issued and outstanding immediately following the completion of the transactions contemplated by this Agreement; and provided further, that each recipient of Ordinary Shares or securities convertible into or exercisable for Ordinary Shares pursuant to this clause (E) shall execute a lock-up agreement substantially in the form of Exhibit A hereto.

(j) If the Representatives, in their discretion, agrees to release or waive the restrictions set forth in a lock-up agreement described in Section 5(i) hereof for an officer or director of the Company and provides the Company with notice of the impending release or waiver at least three business days before the effective date of the release or waiver, the Company agrees to announce the impending release or waiver by a press release substantially in the form of Exhibit B hereto through a major news service at least two business days before the effective date of the release or waiver.

(k) *Reporting Requirements*. The Company, during the period when a Prospectus relating to the Securities is (or, but for the exception afforded by Rule 172, would be) required to be delivered under the 1933 Act, will file all documents required to be filed with the Commission pursuant to the 1934 Act within the time periods required by the 1934 Act and 1934 Act Regulations. Additionally, the Company shall report the use of proceeds from the issuance of the Shares as may be required under Rule 463 under the 1933 Act.

(l) *Issuer Free Writing Prospectuses*. Each of the Company and MeiraGTx UK agrees that, unless it obtains the prior written consent of the Representatives, it will not make any offer relating to the Securities that would constitute an Issuer Free Writing Prospectus or that would otherwise constitute a "free writing prospectus," or a portion thereof, required to be filed by the Company with the Commission or retained by the Company under Rule 433; provided that the Representatives will be deemed to have consented to the Issuer Free Writing Prospectuses listed on Schedule B-2 hereto and any "road show that is a written communication" within the meaning of Rule 433(d)(8)(i) that has been reviewed by the Representatives. Each of the Company and MeiraGTx UK represents that it has treated or agrees that it will treat each such free writing prospectus consented to, or deemed consented to, by the Representatives as an "issuer free writing prospectus," as defined in Rule 433, and that it has complied and will comply with the applicable requirements of Rule 433 with respect thereto, including timely filing with the Commission where required, legending and record keeping. If at any time following issuance of an Issuer Free Writing Prospectus there occurred or occurs an event or development as a result of which such Issuer Free Writing Prospectus conflicted or would conflict with the information contained in the Registration Statement which has not been superseded or modified, any preliminary prospectus or the Prospectus or included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing at that subsequent time, not misleading, the Company and MeiraGTx UK will promptly notify the Representatives and will promptly amend or supplement, at its own expense, such Issuer Free Writing Prospectus to eliminate or correct such conflict, untrue statement or omission.

(o) [Reserved].

(p) *Testing-the-Waters Materials*. If at any time following the distribution of any Written Testing-the-Waters Communication there occurred or occurs an event or development as a result of which such Written Testing-the-Waters Communication included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing at that subsequent time, not misleading, the Company will promptly notify the Representatives and will promptly amend or supplement, at its own expense, such Written Testing-the-Waters Communication to eliminate or correct such untrue statement or omission.

(q) *Emerging Growth Company Status*. The Company will promptly notify the Representatives if the Company ceases to be an Emerging Growth Company at any time prior to the later of (i) completion of the distribution of the Securities within the meaning of the Securities Act and (ii) completion of the 180-day restricted period referred to in Section 3(i).

(r) *Value added tax*. Where any sum (a "**Relevant Sum**") is to be paid or reimbursed to an Underwriter in respect of any cost or expense paid or incurred by such Underwriters and that cost or expense includes an amount in respect of any value added tax (the "**VAT Element**"), the Company shall pay an amount to such Underwriter in respect of the VAT Element determined as follows: (i) if the Relevant Sum constitutes for value added tax purposes reimbursement of the consideration for goods or services supplied to such Underwriter, a sum equal to the proportion of the VAT Element that such Underwriter certifies as representing irrecoverable input tax in the hands of such Underwriter, that certificate to be conclusive save in the case of manifest error; and (ii) if the Relevant Sum constitutes for value added tax purposes the reimbursement of a cost or expense incurred by such Underwriter as agent for the Company, a sum equal to the whole of the VAT Element. Where a sum equal to the VAT Element has been reimbursed to such Underwriter under Section 3(r)(ii), such Underwriter shall provide the Company with a valid tax invoice in respect of the supply to which the Relevant Sum relates, that is to say a tax invoice naming the Company as the recipient of the supply and issued either by such Underwriter or, if such Underwriter has treated the relevant cost or expense as a disbursement for value added tax purposes, by the person making the supply. If the performance by an Underwriter of any of its obligations under this agreement shall represent for value added tax purposes the making by such Underwriter of any supply of goods or services to the Company that is taxable at a positive rate, the Company shall pay to such Underwriter, in addition to the amounts otherwise payable by the Company to such Underwriter pursuant to this agreement (including, without limitation, amounts payable by the Company to an Underwriter pursuant to Sections 3(r)(i) or (ii)), an amount equal to the value added tax chargeable on any such supply, that payment to be made within seven days of such Underwriter requesting the same and against production by such Underwriter of a valid tax invoice.

SECTION 4. Payment of Expenses.

(a) *Expenses*. The Company and MeiraGTx UK, jointly and severally, will pay or cause to be paid all expenses incident to the performance of its obligations under this Agreement, including (i) the preparation, printing and filing of the Registration Statement (including financial statements and exhibits) as originally filed and each amendment thereto, (ii) the preparation, printing and delivery to the Underwriters of copies of each preliminary prospectus, each Issuer Free Writing Prospectus and the Prospectus and any amendments or supplements thereto and any costs associated with electronic delivery of any of the foregoing by the Underwriters to investors, (iii) the preparation, issuance and delivery of the certificates or security entitlements for the Securities to the Underwriters, including any stock or other Transfer Taxes payable upon the sale, issuance or delivery of the Securities to the Underwriters, and the sale of such Securities by the Underwriters to the initial purchasers therefrom in the manner contemplated herein, (iv) the fees and disbursements of the Company's and MeiraGTx UK's counsel, accountants and other advisors, (v) the qualification of the Securities under securities laws in accordance with the provisions of Section 3(e) hereof, including filing fees and the reasonable fees and disbursements of counsel for the Underwriters in connection therewith and in connection with the preparation of the Blue Sky Survey and any supplement thereto, (vi) the fees and expenses of any transfer agent or registrar for the Securities, (vii) the costs and expenses of the Company and MeiraGTx UK relating to investor presentations on any "road show" undertaken in connection with the marketing of the Securities, including without limitation, expenses associated with the production of road show slides and graphics, fees and expenses of any consultants engaged or approved by the Company or MeiraGTx UK in connection with the road show presentations, travel and lodging and commercial airfare expenses of the representatives and officers of the Company or MeiraGTx UK and any such consultants, and 50% of the cost of any private aircraft and other private transportation chartered in connection with the road show, (viii) the filing fees incident to, and the reasonable fees and disbursements of counsel to the Underwriters in connection with, the review by FINRA of the terms of the sale of the Securities, with such legal fees, taken together with the legal fees described in clause (v) above, not to exceed $50,000, (ix) the fees and expenses incurred in connection with the listing of the Securities on the Nasdaq Global Market, and (x) the costs and expenses (including, without limitation, any damages or other amounts payable in connection with legal or contractual liability) associated with the reforming of any contracts for sale of the Securities made by the Underwriters caused by a breach of the representation contained in the third sentence of Section 1(a)(ii), *provided* that any expenses payable under clauses (v) and (viii) above and any expenses related to the remaining 50% of the cost of any private aircraft and other private transportation chartered in connection with the road show described in clause (vii) above are invoiced in a timely manner.

(b) *Termination of Agreement*. If this Agreement is terminated by the Representatives in accordance with the provisions of Section 5, Section 9(a)(i) or (iii) or Section 10 hereof, the Company and MeiraGTx UK shall jointly and severally reimburse the Underwriters for all of their documented out-of-pocket expenses, including the reasonable and documented fees and disbursements of counsel for the Underwriters.

SECTION 5. Conditions of Underwriters' Obligations. The obligations of the several Underwriters hereunder are subject to the accuracy of the representations and warranties of the Company and MeiraGTx UK contained herein or in certificates of any officer of the Company or any of its subsidiaries delivered pursuant to the provisions hereof, to the performance by the Company and MeiraGTx UK of its respective covenants and other obligations hereunder, and to the following further conditions:

(a) *Effectiveness of Registration Statement; Rule 430A Information*. The Registration Statement, including any Rule 462(b) Registration Statement, has become effective and, at the Closing Time, no stop order suspending the effectiveness of the Registration Statement or any post-effective amendment thereto has been issued under the 1933 Act, no order preventing or suspending the use of any preliminary prospectus or the Prospectus has been issued and no proceedings for any of those purposes have been instituted or are pending or, to the Company's knowledge, contemplated; and the Company has complied with each request (if any) from the Commission for additional information. A prospectus containing the Rule 430A Information shall have been filed with the Commission in the manner and within the time frame required by Rule 424(b) without reliance on Rule 424(b)(8) or a post-effective amendment providing such information shall have been filed with, and declared effective by, the Commission in accordance with the requirements of Rule 430A.

(b) *Opinion of Counsel for Company*. At the Closing Time, the Representatives shall have received the opinion and 10b-5 statement, dated the Closing Time, of Latham & Watkins LLP, US counsel for the Company and Latham & Watkins (London) LLP, UK, each in form and substance satisfactory to counsel for the Underwriters, together with signed or reproduced copies of such letter for each of the other Underwriters.

(c) *Opinion of Cayman Islands Counsel for Company*. At the Closing Time, the Representatives shall have received the opinion, dated the Closing Time, of Walkers, Cayman Islands counsel for the Company, in form and substance satisfactory to counsel for the Underwriters, together with signed or reproduced copies of such letter for each of the other Underwriters.

(d) *Opinion of Intellectual Property Counsel for Company*. At the Closing Time, the Representatives shall have received the opinion, dated the Closing Time, of Fox Rothschild LLP, intellectual property counsel for the Company, in form and substance satisfactory to counsel for the Underwriters, together with signed or reproduced copies of such letter for each of the other Underwriters.

(e) *Opinion of US Counsel for Underwriters*. At the Closing Time, the Representatives shall have received the opinion and 10b-5 statement, dated the Closing Time, of Cooley LLP, US counsel for the Underwriters, together with signed or reproduced copies of such letter for each of the other Underwriters, in form and substance reasonably satisfactory to the Representatives.

(f) *Officers' Certificate*. At the Closing Time, there shall not have been, since the date hereof or since the respective dates as of which information is given in the Registration Statement, the General Disclosure Package or the Prospectus, any material adverse change in the condition, financial or otherwise, or in the earnings, business affairs or business prospects of the Company and its subsidiaries considered as one enterprise, whether or not arising in the ordinary course of business, and the Representatives shall have received a certificate of the Chief Executive Officer or the President of the Company and of the chief operating or chief accounting officer of the Company, dated the Closing Time, to the effect that (i) there has been no such material adverse change, (ii) the representations and warranties of the Company in this Agreement are true and correct with the same force and effect as though expressly made at and as of the Closing Time, (iii) the Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied at or prior to the Closing Time, and (iv) no stop order suspending the effectiveness of the Registration Statement under the 1933 Act has been issued, no order preventing or suspending the use of any preliminary prospectus or the Prospectus has been issued and no proceedings for any of those purposes have been instituted or are pending or, to their knowledge, contemplated by the Commission.

(g) *Accountant's Comfort Letter*. At the time of the execution of this Agreement, the Representatives shall have received from Ernst & Young LLP a letter, dated such date, in form and substance satisfactory to the Representatives, together with signed or reproduced copies of such letter for each of the other Underwriters containing statements and information of the type ordinarily included in accountants' "comfort letters" to underwriters with respect to the financial statements and certain financial information contained in the Registration Statement, the General Disclosure Package and the Prospectus.

(h) *Bring-down Comfort Letter*. At the Closing Time, the Representatives shall have received from Ernst & Young LLP a letter, dated as of the Closing Time, to the effect that they reaffirm the statements made in the letter furnished pursuant to subsection (e) of this Section, except that the specified date referred to shall be a date not more than three business days prior to the Closing Time.

(i) *Approval of Listing*. At the Closing Time, the Securities shall have been approved for listing on the Nasdaq Global Market, subject only to official notice of issuance.

(j) *No Objection*. FINRA has confirmed that it has not raised any objection with respect to the fairness and reasonableness of the underwriting terms and arrangements relating to the offering of the Securities.

(k) *Lock-up Agreements*. At the date of this Agreement, the Representatives shall have received an agreement substantially in the form of Exhibit A hereto signed by each officer and director of each of the Company and MeiraGTx UK and each other person and entity agreed to among the Company and the Representatives.

(l) *Corporate Reorganization*. Prior to the closing, the Reorganization Transaction as described above and in the Registration Statement, the General Disclosure Package and the Prospectus under the caption "Prospectus Summary—Corporate Reorganization" shall have occurred.

(m) *Conditions to Subscription of Option Securities*. In the event that the Underwriters exercise their option provided in Section 2(b) hereof to subscribe for all or any portion of the Option Securities, the representations and warranties of the Company contained herein and the statements in any certificates furnished by the Company and any of its subsidiaries hereunder shall be true and correct as of each Date of Delivery and, at the relevant Date of Delivery, the Representatives shall have received:

(i) Officers' Certificate. A certificate, dated such Date of Delivery, of the President or a Vice President of the Company and of the chief operating or chief accounting officer of the Company confirming that the certificate delivered at the Closing Time pursuant to Section 5(d) hereof remains true and correct as of such Date of Delivery.

(ii) Opinion of Counsel for Company. If requested by the Representatives, the opinion and 10b-5 statement of Latham & Watkins LLP, US counsel for the Company, together with the opinion of Latham & Watkins (London) LLP, UK, Walkers, Cayman Islands counsel for the Company, and the opinion of Fox Rothschild LLP, intellectual property counsel for the Company, each in form and substance satisfactory to counsel for the Underwriters, dated such Date of Delivery, relating to the Option Securities to be subscribed for on such Date of Delivery and otherwise to the same effect as the opinions required by Sections 5(b), 5(c) and 5(d) hereof.

(iii) Opinion of Counsel for Underwriters. If requested by the Representatives, the opinion and 10b-5 statement of Cooley LLP, US counsel for the Underwriters, dated such Date of Delivery, relating to the Option Securities to be subscribed for on such Date of Delivery and otherwise to the same effect as the opinion required by Section 5(e) hereof.

(v) Bring-down Comfort Letter. If requested by the Representatives, a letter from Ernst & Young LLP, in form and substance satisfactory to the Representatives and dated such Date of Delivery, substantially in the same form and substance as the letter furnished to the Representatives pursuant to Section 5(g) hereof, except that the "specified date" in the letter furnished pursuant to this paragraph shall be a date not more than three business days prior to such Date of Delivery.

(n) *Additional Documents*. At the Closing Time and at each Date of Delivery (if any) counsel for the Underwriters shall have been furnished with such documents and opinions as they may reasonably require for the purpose of enabling them to pass upon the issuance and sale of the Securities as herein contemplated, or in order to evidence the accuracy of any of the representations or warranties, or the fulfillment of any of the conditions, herein contained; and all proceedings taken by the Company and MeiraGTx UK in connection with the issuance and sale of the Securities as herein contemplated shall be reasonably satisfactory in form and substance to the Representatives and counsel for the Underwriters.

(o) *Termination of Agreement*. If any condition specified in this Section shall not have been fulfilled when and as required to be fulfilled, this Agreement, or, in the case of any condition to the subscription for Option Securities on a Date of Delivery which is after the Closing Time, the obligations of the several Underwriters to subscribe for the relevant Option Securities, may be terminated by the Representatives by notice to the Company at any time at or prior to Closing Time or such Date of Delivery, as the case may be, and such termination shall be without liability of any party to any other party except as provided in Section 4 and except that Sections 1, 6, 7, 8, 14, 15 and 16 shall survive any such termination and remain in full force and effect.

SECTION 6. Indemnification.

(a) *Indemnification of Underwriters*. Each of the Company and MeiraGTx UK agrees, jointly and severally, to indemnify and hold harmless each Underwriter, its affiliates (as such term is defined in Rule 501(b) under the 1933 Act (each, an "Affiliate")), its selling agents and each person, if any, who controls any Underwriter within the meaning of Section 15 of the 1933 Act or Section 20 of the 1934 Act as follows:

(i) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, arising out of any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement (or any amendment thereto), including the Rule 430A Information, or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading or arising out of any untrue statement or alleged untrue statement of a material fact included (A) in any preliminary prospectus, any Issuer Free Writing Prospectus, any Written Testing-the-Waters Communication, the General Disclosure Package or the Prospectus (or any amendment or supplement thereto), or (B) in any materials or information provided to investors by, or with the approval of, the Company or MeiraGTx UK in connection with the marketing of the offering of the Securities ("Marketing Materials"), including any roadshow or investor presentations made to investors by the Company or MeiraGTx UK (whether in person or electronically), or the omission or alleged omission in any preliminary prospectus, Issuer Free Writing Prospectus, any Written Testing-the-Waters Communication, Prospectus or in any Marketing Materials of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading;

(ii) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, to the extent of the aggregate amount paid in settlement of any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or of any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission; provided that (subject to Section 6(d) below) any such settlement is effected with the written consent of the Company or MeiraGTx UK;

(iii) against any and all expense whatsoever, as incurred (including the fees and disbursements of counsel chosen by the Representatives), reasonably incurred in investigating, preparing or defending against any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission, to the extent that any such expense is not paid under (i) or (ii) above;

provided, however, that this indemnity agreement shall not apply to any loss, liability, claim, damage or expense to the extent arising out of any untrue statement or omission or alleged untrue statement or omission made in the Registration Statement (or any amendment thereto), including the Rule 430A Information, the General Disclosure Package or the Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with the Underwriter Information.

(b) *Indemnification of Company, MeiraGTx UK, Directors and Officers*. Each Underwriter severally agrees to indemnify and hold harmless the Company, MeiraGTx UK, its respective directors, each of its respective officers who signed the Registration Statement, and each person, if any, who controls the Company or MeiraGTx UK within the meaning of Section 15 of the 1933 Act or Section 20 of the 1934 Act, against any and all loss, liability, claim, damage and expense described in the indemnity contained in subsection (a) of this Section, as incurred, but only with respect to untrue statements or omissions, or alleged untrue statements or omissions, made in the Registration Statement (or any amendment thereto), including the Rule 430A Information, the General Disclosure Package or the Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with the Underwriter Information.

(c) *Actions against Parties; Notification*. Each indemnified party shall give notice as promptly as reasonably practicable to each indemnifying party of any action commenced against it in respect of which indemnity may be sought hereunder, but failure to so notify an indemnifying party shall not relieve such indemnifying party from any liability hereunder to the extent it is not materially prejudiced as a result thereof and in any event shall not relieve it from any liability which it may have otherwise than on account of this indemnity agreement. In the case of parties indemnified pursuant to Section 6(a) above, counsel to the indemnified parties shall be selected by the Representatives, and, in the case of parties indemnified pursuant to Section 6(b) above, counsel to the indemnified parties shall be selected by the Company or MeiraGTx UK. An indemnifying party may participate at its own expense in the defense of any such action; provided, however, that counsel to the indemnifying party shall not (except with the consent of the indemnified party) also be counsel to the indemnified party. In no event shall the indemnifying parties be liable for fees and expenses of more than one counsel (in addition to any local counsel) separate from their own counsel for all indemnified parties in connection with any one action or separate but similar or related actions in the same jurisdiction arising out of the same general allegations or circumstances. No indemnifying party shall, without the prior written consent of the indemnified parties, settle or compromise or consent to the entry of any judgment with respect to any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or any claim whatsoever in respect of which indemnification or contribution could be sought under this Section 6 or Section 7 hereof (whether or not the indemnified parties are actual or potential parties thereto), unless such settlement, compromise or consent (i) includes an unconditional release of each indemnified party from all liability arising out of such litigation, investigation, proceeding or claim and (ii) does not include a statement as to or an admission of fault, culpability or a failure to act by or on behalf of any indemnified party.

(d) *Settlement without Consent if Failure to Reimburse*. If at any time an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for fees and expenses of counsel, such indemnifying party agrees that it shall be liable for any settlement of the nature contemplated by Section 6(a)(ii) effected without its written consent if (i) such settlement is entered into more than 45 days after receipt by such indemnifying party of the aforesaid request, (ii) such indemnifying party shall have received notice of the terms of such settlement at least 30 days prior to such settlement being entered into and (iii) such indemnifying party shall not have reimbursed such indemnified party in accordance with such request prior to the date of such settlement.

(e) [Reserved].

(f) *Transfer Taxes*. The Company and MeiraGTx UK will jointly and severally indemnify and hold harmless the Underwriters and/or its agents against any Transfer Taxes, including any interest and penalties, incurred in connection with (i) the creation, allotment and issuance of the Securities by the Company or MeiraGTx UK; (ii) the delivery of the Securities by the Company to or for the account of the Underwriters; (iii) the initial sale and delivery (including any agreement for sale or delivery) by the Underwriters of the Securities to purchasers thereof, and (iv) the execution and delivery of this Underwriting Agreement.

SECTION 7. Contribution. If the indemnification provided for in Section 6 hereof is for any reason unavailable to or insufficient to hold harmless an indemnified party in respect of any losses, liabilities, claims, damages or expenses referred to therein, then each indemnifying party shall contribute to the aggregate amount of such losses, liabilities, claims, damages and expenses incurred by such indemnified party, as incurred, (i) in such proportion as is appropriate to reflect the relative benefits received by the Company and MeiraGTx UK, on the one hand, and the Underwriters, on the other hand, from the offering of the Securities pursuant to this Agreement or (ii) if the allocation provided by clause (i) is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) above but also the relative fault of the Company and MeiraGTx UK, on the one hand, and of the Underwriters, on the other hand, in connection with the statements or omissions which resulted in such losses, liabilities, claims, damages or expenses, as well as any other relevant equitable considerations.

The relative benefits received by the Company and MeiraGTx UK, on the one hand, and the Underwriters, on the other hand, in connection with the offering of the Securities pursuant to this Agreement shall be deemed to be in the same respective proportions as the total net proceeds from the offering of the Securities pursuant to this Agreement (before deducting expenses) received by the Company and MeiraGTx UK, on the one hand, and the total underwriting discount received by the Underwriters, on the other hand, in each case as set forth on the cover of the Prospectus, bear to the aggregate initial public offering price of the Securities as set forth on the cover of the Prospectus.

The relative fault of the Company and MeiraGTx UK, on the one hand, and the Underwriters, on the other hand, shall be determined by reference to, among other things, whether any such untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company, MeiraGTx UK or by the Underwriters and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

The Company and the Underwriters agree that it would not be just and equitable if contribution pursuant to this Section 7 were determined by pro rata allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation which does not take account of the equitable considerations referred to above in this Section 7. The aggregate amount of losses, liabilities, claims, damages and expenses incurred by an indemnified party and referred to above in this Section 7 shall be deemed to include any legal or other expenses reasonably incurred by such indemnified party in investigating, preparing or defending against any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, or any claim whatsoever based upon any such untrue or alleged untrue statement or omission or alleged omission.

Notwithstanding the provisions of this Section 7, no Underwriter shall be required to contribute any amount in excess of the underwriting commissions received by such Underwriter in connection with the Shares underwritten by it and distributed to the public.

No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the 1933 Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation.

For purposes of this Section 7, each person, if any, who controls an Underwriter within the meaning of Section 15 of the 1933 Act or Section 20 of the 1934 Act and each Underwriter's Affiliates and selling agents shall have the same rights to contribution as such Underwriter, and each director of the Company or MeiraGTx UK, each officer of the Company or MeiraGTx UK who signed the Registration Statement, and each person, if any, who controls the Company or MeiraGTx UK within the meaning of Section 15 of the 1933 Act or Section 20 of the 1934 Act shall have the same rights to contribution as the Company and MeiraGTx UK. The Underwriters' respective obligations to contribute pursuant to this Section 7 are several in proportion to the number of Initial Securities set forth opposite their respective names in Schedule A hereto and not joint.

SECTION 8. Representations, Warranties and Agreements to Survive. All representations, warranties and agreements contained in this Agreement or in certificates of officers of the Company, MeiraGTx UK or any of its subsidiaries submitted pursuant hereto, shall remain operative and in full force and effect regardless of (i) any investigation made by or on behalf of any Underwriter or its Affiliates or selling agents, any person controlling any Underwriter, its officers or directors or any person controlling the Company or MeiraGTx UK and (ii) delivery of and payment for the Securities.

SECTION 9. Termination of Agreement.

(a) *Termination*. The Representatives may terminate this Agreement, by notice to the Company or MeiraGTx UK, at any time at or prior to the Closing Time (i) if there has been, in the judgment of the Representatives, since the time of execution of this Agreement or since the respective dates as of which information is given in the Registration Statement, the General Disclosure Package or the Prospectus, any material adverse change in the condition, financial or otherwise, or in the earnings, business affairs or business prospects of the Company and its subsidiaries considered as one enterprise, whether or not arising in the ordinary course of business, or (ii) if there has occurred any material adverse change in the financial markets in the United States, United Kingdom or the international financial markets, any outbreak of hostilities or escalation thereof or other calamity or crisis or any change or development involving a prospective change in national or international political, financial or economic conditions, in each case the effect of which is such as to make it, in the judgment of the Representatives, impracticable or inadvisable to proceed with the completion of the offering or to enforce contracts for the sale of the Securities, or (iii) if trading in any securities of the Company has been suspended or materially limited by the Commission or the Nasdaq Global Market, or (iv) if trading generally on the NYSE MKT or the New York Stock Exchange or in the Nasdaq Global Market has been suspended or materially limited, or minimum or maximum prices for trading have been fixed, or maximum ranges for prices have been required, by any of said exchanges or by order of the Commission, FINRA or any other governmental authority, or (v) a material disruption has occurred in commercial banking or securities settlement or clearance services in the United States or United Kingdom or with respect to Clearstream or Euroclear systems in Europe, or (vi) if a banking moratorium has been declared by either Federal or New York authorities or authorities in the United Kingdom.

(b) *Liabilities*. If this Agreement is terminated pursuant to this Section, such termination shall be without liability of any party to any other party except as provided in Section 4 hereof, and provided further that Sections 1, 6, 7, 8, 14, 15 and 16 shall survive such termination and remain in full force and effect.

SECTION 10. Default by One or More of the Underwriters. If one or more of the Underwriters shall fail at the Closing Time or a Date of Delivery to subscribe for the Securities which it or they are obligated to subscribe for under this Agreement (the “Defaulted Securities”), the Representatives shall have the right, within 24 hours thereafter, to make arrangements for one or more of the non-defaulting Underwriters, or any other underwriters, to subscriber for all, but not less than all, of the Defaulted Securities in such amounts as may be agreed upon and upon the terms herein set forth; if, however, the Representatives shall not have completed such arrangements within such 24-hour period, then:

(i) if the number of Defaulted Securities does not exceed 10% of the number of Securities to be subscribed for on such date, each of the non-defaulting Underwriters shall be obligated, severally and not jointly, to subscribe for the full amount thereof in the proportions that their respective underwriting obligations hereunder bear to the underwriting obligations of all non-defaulting Underwriters, or

(ii) if the number of Defaulted Securities exceeds 10% of the number of Securities to be subscribed for on such date, this Agreement or, with respect to any Date of Delivery which occurs after the Closing Time, the obligation of the Underwriters to subscribe, and the Company to sell, the Option Securities to be purchased and sold on such Date of Delivery shall terminate without liability on the part of any non-defaulting Underwriter.

No action taken pursuant to this Section shall relieve any defaulting Underwriter from liability in respect of its default.

In the event of any such default which does not result in a termination of this Agreement or, in the case of a Date of Delivery which is after the Closing Time, which does not result in a termination of the obligation of the Underwriters to purchase and the Company to sell the relevant Option Securities, as the case may be, either the (i) Representatives or (ii) the Company shall have the right to postpone Closing Time or the relevant Date of Delivery, as the case may be, for a period not exceeding seven days in order to effect any required changes in the Registration Statement, the General Disclosure Package or the Prospectus or in any other documents or arrangements. As used herein, the term "Underwriter" includes any person substituted for an Underwriter under this Section 10.

SECTION 11. Notices. All notices and other communications hereunder shall be in writing and shall be deemed to have been duly given if mailed or transmitted by any standard form of telecommunication. Notices to the Underwriters shall be directed to Merrill Lynch at One Bryant Park, New York, New York 10036, attention of Syndicate Department (facsimile: (646) 855-3073), with a copy to ECM Legal (facsimile: (212) 230-8730); notices to the Company and MeiraGTx UK shall be directed to it at 430 East 29th Street, 10th Floor, New York, New York 10016, attention of Alexandria Forbes, Ph.D. or, with a copy to Latham & Watkins LLP, 200 Clarendon Street, 27th Floor, Boston, Massachusetts 02116, attention of Peter N. Handrinos.

SECTION 12. No Advisory or Fiduciary Relationship. Each of the Company and MeiraGTx UK acknowledges and agrees that (a) the subscription and sale of the Securities pursuant to this Agreement, including the determination of the initial public offering price of the Securities and any related discounts and commissions, is an arm's-length commercial transaction between the Company and MeiraGTx UK, on the one hand, and the several Underwriters, on the other hand, (b) in connection with the offering of the Securities and the process leading thereto, each Underwriter is and has been acting solely as a principal and is not the agent or fiduciary of the Company, MeiraGTx UK, any of its respective subsidiaries or their respective shareholders, creditors, employees or any other party, (c) no Underwriter has assumed or will assume an advisory or fiduciary responsibility in favor of the Company or MeiraGTx UK with respect to the offering of the Securities or the process leading thereto (irrespective of whether such Underwriter has advised or is currently advising the Company, MeiraGTx UK or any of its respective subsidiaries on other matters) and no Underwriter has any obligation to the Company or MeiraGTx UK with respect to the offering of the Securities except the obligations expressly set forth in this Agreement, (d) the Underwriters and their respective affiliates may be engaged in a broad range of transactions that involve interests that differ from those of the Company or MeiraGTx UK and (e) the Underwriters have not provided any legal, accounting, regulatory or tax advice with respect to the offering of the Securities and the Company and MeiraGTx UK has consulted its own respective legal, accounting, regulatory and tax advisors to the extent it deemed appropriate.

SECTION 13. Parties. This Agreement shall each inure to the benefit of and be binding upon the Underwriters,the Company, MeiraGTx UK and their respective successors. Nothing expressed or mentioned in this Agreement is intended or shall be construed to give any person, firm or corporation, other than the Underwriters, the Company, MeiraGTx UK and their respective successors and the controlling persons and officers and directors referred to in Sections 6 and 7 and their heirs and legal representatives, any legal or equitable right, remedy or claim under or in respect of this Agreement or any provision herein contained. This Agreement and all conditions and provisions hereof are intended to be for the sole and exclusive benefit of the Underwriters, the Company, MeiraGTx UK and their respective successors, and said controlling persons and officers and directors and their heirs and legal representatives, and for the benefit of no other person, firm or corporation. No purchaser of Securities from any Underwriter shall be deemed to be a successor by reason merely of such purchase.

SECTION 14. Trial by Jury. The Company and MeiraGTx UK (each on its behalf and, to the extent permitted by applicable law, on behalf of its shareholders and affiliates) and each of the Underwriters hereby irrevocably waives, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to this Agreement or the transactions contemplated hereby.

SECTION 15. GOVERNING LAW. THIS AGREEMENT AND ANY CLAIM, CONTROVERSY OR DISPUTE ARISING UNDER OR RELATED TO THIS AGREEMENT SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF, THE STATE OF NEW YORK WITHOUT REGARD TO ITS CHOICE OF LAW PROVISIONS.

SECTION 16. Consent to Jurisdiction; Waiver of Immunity. Any legal suit, action or proceeding arising out of or based upon this Agreement or the transactions contemplated hereby ("Related Proceedings") shall be instituted in (i) the federal courts of the United States of America located in the City and County of New York, Borough of Manhattan or (ii) the courts of the State of New York located in the City and County of New York, Borough of Manhattan (collectively, the "Specified Courts"), and each party irrevocably submits to the exclusive jurisdiction (except for proceedings instituted in regard to the enforcement of a judgment of any such court (a "Related Judgment"), as to which such jurisdiction is non-exclusive) of such courts in any such suit, action or proceeding. Service of any process, summons, notice or document by mail to such party's address set forth above shall be effective service of process for any suit, action or other proceeding brought in any such court. The parties irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the Specified Courts and irrevocably and unconditionally waive and agree not to plead or claim in any such court that any such suit, action or other proceeding brought in any such court has been brought in an inconvenient forum. Each party not located in the United States irrevocably appoints MeiraGTx LLC as its agent to receive service of process or other legal summons for purposes of any such suit, action or proceeding that may be instituted in any state or federal court in the City and County of New York. With respect to any Related Proceeding, each party irrevocably waives, to the fullest extent permitted by applicable law, all immunity (whether on the basis of sovereignty or otherwise) from jurisdiction, service of process, attachment (both before and after judgment) and execution to which it might otherwise be entitled in the Specified Courts, and with respect to any Related Judgment, each party waives any such immunity in the Specified Courts or any other court of competent jurisdiction, and will not raise or claim or cause to be pleaded any such immunity at or in respect of any such Related Proceeding or Related Judgment, including, without limitation, any immunity pursuant to the United States Foreign Sovereign Immunities Act of 1976, as amended.

SECTION 17. Judgment Currency. The obligations of the Company and MeiraGTx UK pursuant to this Agreement in respect of any sum due to any Underwriter shall, notwithstanding any judgment in a currency other than United States dollars, not be discharged until the first business day, following receipt by such Underwriter of any sum adjudged to be so due in such other currency, on which (and only to the extent that) such Underwriter may in accordance with normal banking procedures purchase United States dollars with such other currency; if the United States dollars so purchased are less than the sum originally due to such Underwriter hereunder, each of the Company and MeiraGTx UK agrees, as a separate obligation and notwithstanding any such judgment, to jointly and severally indemnify such Underwriter against such loss.

SECTION 18. Gross Up. All payments made by the Company or MeiraGTx UK under this Agreement, if any, will be made without withholding or deduction for or on account of any present or future taxes, duties, assessments or governmental charges of whatever nature (other than taxes on net income) imposed or levied by any jurisdiction or any political subdivision or any taxing authority thereof or therein unless the Company or MeiraGTx UK is or becomes required by law to withhold or deduct such taxes, duties, assessments or other governmental charges. In such event, the Company or MeiraGTx UK shall pay such additional amounts as will result, after such withholding or deduction, in the receipt by each Underwriter and each person controlling any Underwriter, as the case may be, of the amounts that would otherwise have been received had no withholding or deduction been made.

SECTION 19. TIME. TIME SHALL BE OF THE ESSENCE OF THIS AGREEMENT. EXCEPT AS OTHERWISE SET FORTH HEREIN, SPECIFIED TIMES OF DAY REFER TO NEW YORK CITY TIME.

SECTION 20. Counterparts. This Agreement may be executed in any number of counterparts, each of which shall be deemed to be an original, but all such counterparts shall together constitute one and the same Agreement.

SECTION 21. Effect of Headings. The Section headings herein are for convenience only and shall not affect the construction hereof.

If the foregoing is in accordance with your understanding of our agreement, please sign and return to the Company and MeiraGTx UK a counterpart hereof, whereupon this instrument, along with all counterparts, will become a binding agreement among the Underwriters, the Company and MeiraGTx UK in accordance with its terms.

Very truly yours,

MeiraGTx Holdings plc

By ______________________________
Title:

MeiraGTx Limited

By ______________________________
Title:

CONFIRMED AND ACCEPTED,
as of the date first above written:

MERRILL LYNCH, PIERCE, FENNER & SMITH
INCORPORATED

By ______________________________
Authorized Signatory

BARCLAYS CAPITAL INC.

By ______________________________
Authorized Signatory

Each, for itself and as a Representative of the other Underwriters named in Schedule A hereto.

SCHEDULE A

The initial public offering price per share for the Securities shall be $[•].

The subscription price per share for the Securities to be paid by the several Underwriters shall be $[•], being an amount equal to the initial public offering price set forth above less $[•] per share, subject to adjustment in accordance with Section 2(b) for dividends or distributions declared by the Company and payable on the Initial Securities but not payable on the Option Securities.

| Name of Underwriter | Number of Initial Securities |
|---|---|
| Merrill Lynch, Pierce, Fenner & Smith Incorporated | |
| Barclays Capital Inc. | |
| Evercore Inc. | |
| Chardan Capital Markets LLC | |
| Total | [•] |

SCHEDULE B-1

Pricing Terms

1. The Company is selling [•] Ordinary Shares.
2. The Company has granted an option to the Underwriters, severally and not jointly, to subscribe for up to an additional [•] Ordinary Shares.
3. The initial public offering price per share for the Securities shall be $[•].

SCHEDULE B-2

Free Writing Prospectuses

[•]

Exhibit A

[•], 2018

MeiraGTX Limited
430 East 29th Street, 15th Floor
New York, New York 10016

Merrill Lynch, Pierce, Fenner & Smith
Incorporated
Barclays Capital Inc.

as Representatives of the several
Underwriters to be named in the
within-mentioned Underwriting Agreement

c/o Merrill Lynch, Pierce, Fenner & Smith
Incorporated
One Bryant Park
New York, New York 10036

c/o Barclays Capital Inc.
745 Seventh Avenue
New York, New York 10019

Re: Proposed Public Offering

Dear Sirs:

The undersigned, a stockholder, an officer and/or director of MeiraGTX Limited, a company organized under the laws of England and Wales (or, as the case may be, any holding company of the same incorporated under the laws of the Cayman Islands) (the “Company”), understands that Merrill Lynch, Pierce, Fenner & Smith Incorporated (“Merrill Lynch”) and Barclays Capital Inc. (together with Merrill Lynch, the “Representatives”) propose to enter into an underwriting agreement (the “Underwriting Agreement”) with the Company and the other underwriters party thereto providing for the public offering (the “Public Offering”) of the Company’s ordinary shares (the “Ordinary Shares”). In recognition of the benefit that such an offering will confer upon the undersigned as a stockholder, an officer and/or director of the Company, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the undersigned agrees with each underwriter to be named in the Underwriting Agreement that, during the period beginning on the date hereof and ending on the date that is 180 days from the date of the Underwriting Agreement, the undersigned will not, without the prior written consent of the Representatives, (i) directly or indirectly, 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 or otherwise transfer or dispose of any Ordinary Shares or any securities convertible into or exercisable or exchangeable for Ordinary Shares, whether now owned or hereafter acquired by the undersigned or with respect to which the undersigned has or hereafter acquires the power of disposition (collectively, the “Lock-Up Securities”), or (ii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the Lock-Up Securities, whether any such swap or transaction is to be settled by delivery of Ordinary Shares or other securities, in cash or otherwise. If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing provisions shall be equally applicable to any issuer-directed Securities the undersigned may purchase in the offering.

If the undersigned is an officer or director of the Company, (1) the Representatives agree that, at least three business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of shares of the Ordinary Shares, they will notify the Company of the impending release or waiver, and (2) the Company has agreed in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the effective date of the release or waiver. Any release or waiver granted by the Representatives hereunder to any such officer or director shall only be effective two business days after the publication date of such press release. The provisions of this paragraph will not apply if (i) the release or waiver is effected solely to permit a transfer not for consideration and (ii) the transferee has agreed in writing to be bound by the same terms described in this letter to the extent and for the duration that such terms remain in effect at the time of the transfer.

Notwithstanding the foregoing, and subject to the conditions below, the undersigned may transfer or otherwise dispose of the Lock-Up Securities without the prior written consent of the Representatives, provided that (1) the Representatives receive a signed lock-up agreement for the balance of the lockup period from each donee, trustee, distributee, or transferee, as the case may be, (2) (a) in the case of clauses (i) through (v) below, such transfers are not dispositions for value or required to be reported with the Securities and Exchange Commission on Form 4 in accordance with Section 16 of the Securities Exchange Act of 1934, as amended, and (b) in the case of clauses (vi) through (ix) below, any such required Form 4 shall state the reason for such transfer, and (3) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers:

(i) as a *bona fide* gift or gifts; or

(ii) to any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned (for purposes of this lock-up agreement, "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin); or

(iii) as a distribution to limited or general partners, stockholders or members of the undersigned; or

(iv) to the undersigned's affiliates or to any investment fund or other entity controlled or managed by the undersigned; or

(v) by will or intestacy; or

(vi) to the Company in connection with the exercise of options, warrants or other rights to acquire Ordinary Shares or any security convertible into or exercisable for Ordinary Shares of the Company by way of net exercise and/or to cover withholding tax obligations in connection with such exercise pursuant to an employee benefit plan, option, warrant or other right disclosed in the prospectus for the Public Offering, provided that any such shares issued upon exercise of such option, warrant or other right shall be subject to the restrictions set forth herein; or

(vii) pursuant to a court order or settlement agreement related to the distribution of assets in connection with the dissolution of a marriage or civil union; or

(viii) to the Company pursuant to agreements under which the Company has the option to repurchase such shares or a right of first refusal with respect to transfers of such shares upon termination of service of the undersigned; or

(ix) pursuant to the automatic conversion of outstanding preferred shares of the Company into Ordinary Shares of the Company in connection with the Public Offering, *provided* that the Ordinary Shares received upon such conversion shall be subject to the restrictions set forth herein; or

(x) to a *bona fide* third party pursuant to a merger, consolidation, tender offer or other similar transaction made to all holders of Ordinary Shares and involving a Change of Control of the Company and approved by the Company's board of directors; *provided* that, in the event that such Change of Control is not completed, the undersigned's Lock-Up Securities shall remain subject to the restrictions contained herein. "Change of Control" shall mean the transfer (whether by tender offer, merger, consolidation or other similar transaction), in one transaction or a series of related transactions, to a person or group of affiliated persons (other than an underwriter pursuant to the Public Offering), of the Company's voting securities if, after such transfer, such person or group of affiliated persons would hold more than 50% of the outstanding voting securities of the Company (or the surviving entity).

Furthermore, the undersigned may sell shares of Ordinary Shares of the Company purchased by the undersigned on the open market following the Public Offering if and only if (i) such sales are not required to be reported in any public report or filing with the Securities and Exchange Commission, or otherwise and (ii) the undersigned does not otherwise voluntarily effect any public filing or report regarding such sales.

The undersigned also agrees and consents to the entry of stop transfer instructions with the Company's transfer agent and registrar against the transfer of the Lock-Up Securities except in compliance with the foregoing restrictions.

Notwithstanding the foregoing, the undersigned may establish a trading plan pursuant to Rule 10b5-1 under the Securities Exchange Act of 1934, as amended, provided, that (i) the undersigned is not required to and does not otherwise effect any public filing or report regarding the establishment of such plan during the Lock-Up Period and (ii) no sales are made during the Lock-Up Period pursuant to such plan.

In addition, the undersigned hereby waives any rights the undersigned may have to require registration of Ordinary Shares in connection with the filing of a registration statement relating to the Public Offering. The undersigned further agrees that, for the Lock-Up Period, the undersigned will not, without the prior written consent of the Representatives, make any demand for, or exercise any right with respect to, or file or cause to be filed any registration statement with respect to, the registration of Ordinary Shares or any securities convertible into or exercisable or exchangeable for Ordinary Shares, or warrants or other rights to purchase Ordinary Shares or any such securities. In addition, the undersigned hereby waives any and all preemptive rights, participation rights (including concurrent private placement rights), resale rights, rights of first refusal and similar rights that the undersigned may have in connection with the Public Offering or with any issuance or sale by the Company of any equity or other securities before the Public Offering, except for any such rights as have been heretofore duly exercised.

This agreement (and for the avoidance of doubt, the Lock-Up Period described herein) and related restrictions shall automatically terminate upon the earliest to occur, if any, of (i) the Company advising the Representatives in writing prior to the execution of the Underwriting Agreement that it has determined not to proceed with the Public Offering, (ii) the termination of the Underwriting Agreement before the sale of any Ordinary Shares to the underwriters, (iii) the registration statement filed with the SEC with respect to the Public Offering contemplated by the Underwriting Agreement is withdrawn or (iv) September 30, 2018, in the event the closing of the Public Offering shall not have occurred on or before such date (provided, that the Company may by written notice to the undersigned prior to September 30, 2018 extend such date for a period of up to an additional three months).

Exhibit B

FORM OF PRESS RELEASE
TO BE ISSUED PURSUANT TO SECTION 3(j)

[MeiraGTx Holdings plc]
[•], 2018

[MeiraGTx Holdings plc] (the "Company") announced today that BofA Merrill Lynch, the lead book-running manager in the Company's recent public sale of [•] Ordinary Shares, is [waiving] [releasing] a lock-up restriction with respect to [•] shares of the Company's Ordinary Shares held by [certain officers or directors] [an officer or director] of the Company. The [waiver] [release] will take effect on [•], 2018, and the [•] shares of the Company's Ordinary Shares may be sold on or after such date.

**This press release is not an offer for sale of the securities in the United States or in any other jurisdiction where such offer is prohibited, and such securities may not be offered or sold in the United States absent registration or an exemption from registration under the United States Securities Act of 1933, as amended.**

**Exhibit 3.2**

**THE COMPANIES LAW (AS AMENDED)**

**COMPANY LIMITED BY SHARES**

**AMENDED AND RESTATED**

**MEMORANDUM OF ASSOCIATION**

**OF**

**MEIRAGTX HOLDINGS PLC**

**(ADOPTED BY SPECIAL RESOLUTION DATED [        ])**

**THE COMPANIES LAW (AS AMENDED)**

**COMPANY LIMITED BY SHARES**

**AMENDED AND RESTATED**

**MEMORANDUM OF ASSOCIATION**

**OF**

**MEIRAGTX HOLDINGS PLC**

**(ADOPTED BY SPECIAL RESOLUTION DATED [        ])**

1. The name of the company is MeiraGTx Holdings plc (the "**Company**").

2. The registered office of the Company will be situated at the offices of Walkers Corporate Limited, Cayman Corporate Centre, 27 Hospital Road, George Town, Grand Cayman KY1-9008, Cayman Islands or at such other location as the Directors may from time to time determine.

3. The objects for which the Company is established are unrestricted and the Company shall have full power and authority to carry out any object not prohibited by any law as provided by Section 7(4) of the Companies Law (as amended) of the Cayman Islands (the "**Act**").

4. The Company shall have and be capable of exercising all the functions of a natural person of full capacity irrespective of any question of corporate benefit as provided by Section 27(2) of the Act.

5. The Company will not trade in the Cayman Islands with any person, firm or corporation except in furtherance of the business of the Company carried on outside the Cayman Islands; provided that nothing in this section shall be construed as to prevent the Company effecting and concluding contracts in the Cayman Islands, and exercising in the Cayman Islands all of its powers necessary for the carrying on of its business outside the Cayman Islands.

6. The liability of the shareholders of the Company is limited to the amount, if any, unpaid on the shares respectively held by them.

7. The capital of the Company is US$50,000 divided into 5,000,000,000 shares with a nominal or par value of **US$0.00001** provided always that subject to the Act and the Articles of Association the Company shall have power to redeem or purchase any of its shares and to sub-divide or consolidate the said shares or any of them and to issue all or any part of its capital whether original, redeemed, increased or reduced with or without any preference, priority, special privilege or other rights or subject to any postponement of rights or to any conditions or restrictions whatsoever and so that unless the conditions of issue shall otherwise expressly provide every issue of shares whether stated to be ordinary, preference or otherwise shall be subject to the powers on the part of the Company hereinbefore provided.

8. The Company may exercise the power contained in Section 206 of the Act to deregister in the Cayman Islands and be registered by way of continuation in some other jurisdiction.

# THE COMPANIES LAW (AS AMENDED)

# AMENDED AND RESTATED

# ARTICLES OF ASSOCIATION

# OF

# MEIRAGTX HOLDINGS PLC

**(ADOPTED BY SPECIAL RESOLUTION DATED [        ])**

**INDEX**

**COMPANIES LAW (AS AMENDED)**

**COMPANY LIMITED BY SHARES**

**AMENDED AND RESTATED**

**ARTICLES OF ASSOCIATION**

**OF**

**MEIRAGTX HOLDINGS PLC ("Company")**

**(ADOPTED BY SPECIAL RESOLUTION DATED [ ])**

## PART 1: PRELIMINARY AND LIMITATION OF LIABILITY

**1. Regulations and Articles not to apply**

**1.1** The Regulations contained or incorporated in Table 'A' in the First Schedule of the Act shall not apply to the Company and the following Articles shall comprise the Articles of Association of the Company.

**2. Defined terms and interpretation**

2.1 In these Articles, unless the context requires otherwise:

**"Act"** means the Companies Law (as amended) of the Cayman Islands;

**"Acting in Concert"** has the meaning given to it in The City Code on Takeovers and Mergers published by the UK Panel on Takeovers and Mergers (as amended from time to time);

"**Adoption Date**" means [ ] 2018;

**"Affiliate"** means, with respect to a person, any legal entity that owns, directly or indirectly, at least 50% of the voting securities of that person; has at least 50% of its voting securities owned, directly or indirectly, by that person; or has at least 50% of its voting securities owned, directly or indirectly, by a legal entity that owns, directly or indirectly, at least 50% of the voting securities of that person;

**"Albion**" means Albion Capital Group LLP for and on behalf of UCL Technology Fund and for the purposes of Articles 28 and 31, Albion shall be deemed to include UCLB (and each of their Permitted Transferees) and for such purposes, any reference to Albion's shareholding in the Company shall be to their aggregate shareholding;

**"Alternate Director"** has the meaning given in Article 24.1;

**"Appointor"** has the meaning given in Article 24.1;

"**Approved Share Sale**" means a Share Sale approved by: (i) the Board; (ii) the holders of at least 50.5% of the C Shares then in issue; and (iii) the holders of at least 50.5% of the A Shares then in issue;

**"Articles"** means the Company's Articles of association;

**"A Shares"** means the A ordinary shares of US$0.00001 each in the capital of the Company;

**“Asset Sale”** means the sale by the Company of all or substantially all of its business and assets, through one or a series of transactions;

**“Athena Founders”** means Robin Ali, Stuart Naylor, James Bainbridge, Alexander Smith and UCLB, being shareholders of the Company on the Adoption Date;

“**Board**” means the board of Directors, from time to time;

“**Business Day**” means a day (except a Saturday or Sunday) on which banks are generally open for business in London, England;

**“Chairman”** has the meaning given in Article 12.2;

**“Connected”** means, with respect to a Director, the following persons:

(a) members of the Director’s family, being:

(i) the Director’s spouse or civil partner;

(ii) any other person (whether of a different sex or the same sex) with whom the Director lives as partner in an enduring family relationship (except for if the other person is the Director’s grandparent or grandchild, sister, brother, aunt or uncle, or nephew or niece);

(iii) the Director’s children or step-children; any children or step-children of person within paragraph (ii) (and who are not children or step-children of the Director) who live with the Director and have not attained the age of 18; or

(iv) the Director’s parents;

(b) a body corporate with which the Director is connected, meaning if a Director and the persons Connected with him together:

(i) are interested in shares comprised in the equity share capital of that body corporate of a nominal value equal to at least 20% of that share capital; or

(ii) are entitled to exercise or control the exercise of more than 20% of the voting power at any general meeting of that body (voting power for this purpose includes voting power whose exercise is controlled by a body corporate Controlled by him, but excludes any voting rights attaching to shares in a company held as treasury shares);

(c) a person acting in his capacity as trustee of a trust:

(i) the beneficiaries of which should include the Director or a person who by virtue of (a) or (b) is connected with him; or

(ii) the terms of which confer a power on the trustees that may be exercised for the benefit of the Director or any such person,

other than a trust for the purposes of an employees’ share scheme or a pension scheme;

(d) a person acting in his capacity as partner:

(i) of the Director; or

(ii) of a person who, by virtue of (a), (b) or (c) is connected with that Director; or

(e) a firm that is a legal person under the law by which it is governed and in which:

(i) the Director is a partner;

(ii) a partner is a person who, by virtue of (a), (b) or (c) is connected with the Director; or

(iii) a partner is a firm in which the Director is a partner or in which there is a partner who, by virtue of (a), (b) or (c) is connected with the Director.

References to a person connected with a Director do not include a person who is himself a Director.

**"Connected Person"** has the meaning given to it in section 1122 of the UK Corporation Tax Act 2010;

**"Conversion Rate"** means a conversion of one C Share into one A Share, subject to such adjustments as may be approved by the board of directors as being required to take account of any bonus issue, share subdivision, consolidations, capitalisations or other reorganisation of the Company's share capital;

"**C Share Starting Price**" means US$2.70 in respect of each C Share;

**"C Shares"** means the convertible preferred C shares of US$0.00001 each in the capital of the Company;

**"Diluted Share Capital** " means, at the relevant time, the aggregate of the issued Shares or Other Securities in issue, including if all C Shares were converted and reclassified into A Shares by applying the Conversion Rate applicable on such date in accordance with these Articles;

**"Director"** means a director for the time being of the Company, and includes any person for the time being occupying the position of Director, by whatever name called;

**"Eligible Director"** means:

(a) in relation to a decision at a Directors' meeting, a Director who is to be counted as participating for quorum and voting purposes in the decision at the meeting; and

(b) in relation to a Directors' written resolution, a Director who would have been counted as participating for quorum and voting purposes in the decision had the resolution or matter been proposed as a resolution at a Directors' meeting;

**"Exit"** means an Asset Sale, a Qualified IPO or a Sale;

**"Family Member"** means in relation to any Member, as at the Adoption Date, the Member's spouse or estate for the time being, parent, and all lineal descendants of that Member (including for this purpose any step-child, adopted child or illegitimate child of the Member or his lineal descendants) or any person who for the time being is married to or of any such lineal descendant but no lineal descendant may be a Family Member whilst a minor;

**"Family Trust"** means a trust (whether arising under a settlement, declaration of trust, testamentary disposition or on an intestacy) under which the only persons being (or capable of being) beneficiaries are the Member, as at the Adoption Date and/or his Family Members, and no power of control over the voting powers conferred by such Shares is exercisable at any time by or subject to the consent of any person other than the trustees as trustees or such Member or his Family Member;

"**Fund Manager**" means a person whose principal business is to make, manage or advise upon investments in securities;

**"Kadmon"** means Kadmon Corporation, LLC;

"**Member**" means any Person holding Shares from time to time;

"**Member of the same Fund Group**" means, if the Member is a fund, partnership, company, syndicate or other entity whose business is managed by a Fund Manager (an "**Investment Fund**") or is a nominee of that Investment Fund:

(a) any participant or partner in or member of any such Investment Fund or the holders of any unit trust which is a participant or partner in or member of any Investment Fund (but only in connection with the dissolution of the Investment Fund or any distribution of assets of the Investment Fund pursuant to the operation of the Investment Fund in the ordinary course of business);

(b) any Investment Fund managed or advised by that Fund Manager or any Affiliate of that Fund Manager; or

(c) any trustee, nominee or custodian of such Investment Fund and vice versa;

**"Ordinary Resolution"** means a resolution:

(a) passed by a simple majority of such Members as, being entitled to do so, vote in person or, where proxies are allowed, by proxy at a general meeting of the Company and where a poll is taken regard shall be had in computing a majority to the number of votes to which each Member is entitled; or

(b) approved in writing by all of the Members entitled to vote at a general meeting of the Company in one or more instruments each signed by one or more of the Members and the effective date of the resolution so adopted shall be the date on which the instrument, or the last of such instruments, if more than one, is executed.

**"Other Securities**" means preferred equity certificates, convertible preferred equity certificates, shareholder debt, loan notes, loans and/or preference shares (in each case other than any third party indebtedness);

"**Person**" means any natural person, partnership, corporation, limited liability company, trust, estate, association, unincorporated organization or other entity or association;

**"Permitted Issue"** means any of the following:

(a) grant of options, and issue of equity shares pursuant to the exercise thereof, to employees, directors, advisors or consultants of the Company or any of its subsidiaries, in connection with, or pursuant to, any plan, agreement or arrangement approved by the Directors or a duly constituted committee of the board of Directors;

(b) issue of equity shares to employees, directors or consultants of any member of the Company's group, in respect of incentivisation, retention and remuneration, as approved by the Directors or a duly constituted committee of the board of Directors (subject to reasonable and customary caps);

(c) issue of equity shares pursuant to any agreement entered into prior to the Adoption Date;

(d) issue of equity shares pursuant to any warrants, options or other instruments convertible into or exchangeable for equity shares issued after the date of these Articles, provided that the pre-emptive rights established by Article 29 applied with respect to the initial sale or grant by the Company of such warrants, options or other instruments;

(e) issue of equity shares (whether pursuant to any warrants, options or other instruments convertible into or exchangeable for equity shares, or otherwise) pursuant to the acquisition of another business pursuant to a merger, consolidation, acquisition, reorganisation, acquisition of substantially all of the assets or similar business combination or pursuant to any collaboration, partnering or other arrangement, provided such transaction is approved by the Directors;

(f) issue of equity shares (whether pursuant to any warrants, options or other instruments convertible into or exchangeable for equity shares, or otherwise) as a dividend or distribution payable to holders of Shares;

(g) issue of equity shares (whether pursuant to any warrants, options or other instruments convertible into or exchangeable for equity shares, or otherwise) pursuant to any sub-division or reclassification of Shares;

(h) issue of equity shares (whether pursuant to any warrants, options or other instruments convertible into or exchangeable for equity shares, or otherwise) upon the conversion or exchange of any option or convertible security, in each case provided such issuance is pursuant to the terms of such option or convertible security;

(i) issue of equity shares (whether pursuant to any warrants, options or other instruments convertible into or exchangeable for equity shares, or otherwise) to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, venture debt facility, equipment leasing or real property leasing transaction approved by the Directors;

(j) issue of equity shares (whether pursuant to any warrants, options or other instruments convertible into or exchangeable for equity shares, or otherwise) to suppliers or third party service providers in connection with the provision of goods or services pursuant to transactions approved by the Directors;

(k) issue of equity shares (whether pursuant to any warrants, options or other instruments convertible into or exchangeable for equity shares, or otherwise) in connection with sponsored research, collaboration, technology license, development, OEM, marketing or other similar agreements or strategic partnerships approved by the Directors;

(l) issue of up to an aggregate amount of 45,000,000 C Shares;

(m) issue of equity shares in relation to a Qualified IPO; or

(n) issue of equity shares and C Shares on the transfer to the Company of an equivalent amount of equity shares and C shares in MeiraGTx Limited.

**"Proceeds of Sale**" means the consideration payable (including any deferred consideration) whether in cash or otherwise to those Members selling Shares pursuant to a Sale (net of all costs, fees charges and expenses of the Members who are selling their Shares and of the Company incurred in connection with the Sale, in each case as approved by the Board);

**"Proxy Notice"** has the meaning given in Article 49.1;

**"Qualified IPO"** means either (a) 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 C Shares only, less than $40,000,000; or (b) 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, S-1 or equivalent admission document;

**"Qualifying C Holder"** means (i) a Member holding at least the number of C Shares which, if such C Shares were converted and reclassified into A Shares, would constitute not less than 2 per cent. of the Diluted Share Capital and who is an accredited investor as defined in Regulation D under the Securities Act; and (ii) Albion, for as long as Albion holds Shares;

**"Register"** means the register of Members of the Company required to be kept pursuant to the Act;

**"Sale"** means unconditional completion of any of: (a) a Share Sale; or (b) a sale pursuant to Article 33;

"**Securities Act**" means the United States Securities Act of 1933, as amended;

**"Seller"** means a Member giving a Transfer Notice;

**"Shares"** means the A Shares and the C Shares and any other equity shares in the capital of the Company;

**"Share Sale"** means any sale of Shares of the Company, in a single transaction or series of related transactions, representing at least 50% of the voting power of the Company (but excluding a Qualified IPO or any transaction or series of transactions entered into principally for bona fide equity financing purposes in which the Company issues new securities primarily for cash, the cancellation or conversion of indebtedness of the Company, or the combination thereof for the purpose of financing the operations and business of the Company);

**"Shareholders' Agreement"** means the shareholders' agreement in respect of the Company dated [ ] 2018, as amended from time to time;

**"Special Resolution"** means a special resolution of the Company passed in accordance with the Act, being a resolution:

(a) passed by a majority of not less than 75% of such Members as, being entitled to do so, vote in person or, where proxies are allowed, by proxy at a general meeting of the Company of which notice specifying the intention to propose the resolution as a special resolution has been duly given and where a poll is taken regard shall be had in computing a majority to the number of votes to which each Member is entitled; or

(b) approved in writing by all of the Members entitled to vote at a general meeting of the Company in one or more instruments each signed by one or more of the Member and the effective date of the special resolution so adopted shall be the date on which the instrument or the last of such instruments, if more than one, is executed.

**"subsidiary"** means an entity which another company, its "holding company":

(a) holds a majority of the voting rights in; or

(b) is a member of and has the right to appoint or remove a majority of its board of directors; or

(c) is a member of and controls alone, pursuant to an agreement with other members, a majority of the voting rights in,

or an entity which is a subsidiary of a company that is itself a subsidiary of that other company.

**"UCLB"** means UCL Business PLC (registered number 2776963); and

**"writing"** and **"written"** means the representation or reproduction of words, symbols or other information in a visible form by any method or combination of methods, whether sent or supplied in electronic form or otherwise.

2.2 Unless the context requires otherwise, other words or expressions contained in these Articles bear the same meaning as in the Act as in force on the date when these Articles become binding on the Company.

2.3 If, and for so long as, the Company has only one Director, all references in these Articles to **"Directors"** (other than in those provisions which govern the decision-making by Directors (Articles 7 to 14) and Directors' interests (Articles 15 to 19)) shall be construed as a reference to that sole Director.

2.4 References in these Articles to the day on which a notice is given are to the day on which the notice is deemed received in accordance with Article 57.

2.5 References to numbered "Articles" are references to numbered provisions in these Articles.

2.6 Headings in these Articles are used for convenience only and shall not affect the meaning of these Articles.

**3. Liability of Members and Register of Members**

3.1 The liability of the Members of the Company is limited to the amount, if any, unpaid on the Shares held by them.

3.2 The Directors shall keep, or cause to be kept, the Register at such place or (subject to compliance with the Act and these Articles) places as the Directors may from time to time determine. In the absence of any such determination, the Register shall be kept at the Registered Office of the Company.

3.3 Subject to the remaining provisions of these Articles, the Directors may issue fractions of a Share and, if so issued, a fraction of a Share shall be subject to and carry the corresponding fraction of liabilities (whether with respect to nominal or par value, premium, contributions, calls or otherwise), limitations, preferences, privileges, qualifications, restrictions, rights (including, without prejudice to the generality of the foregoing, voting and participation rights) and other attributes of a whole Share. If more than one fraction of a Share of the same class is issued to or acquired by the same Member such fractions shall be accumulated.

PART 2: OFFICERS

## DIRECTORS' POWERS AND RESPONSIBILITIES

**4. Directors' general authority**

Subject to the Articles, the Directors are responsible for the management of the Company's business, for which purpose they may exercise all the powers of the Company.

**5. Directors may delegate**

5.1 Subject to the Articles, the Directors may delegate any of the powers which are conferred on them under the Articles and which are not specifically reserved to the Directors only:

5.1.1 to such person or committee;

5.1.2 by such means (including by power of attorney);

5.1.3 to such an extent;

5.1.4 in relation to such matters or territories; and

5.1.5 on such terms and conditions,

as they think fit.

5.2 The Directors may revoke any delegation in whole or part, or alter its terms and conditions.

**6. Committees**

6.1 Committees to which the Directors delegate any of their powers must follow procedures which are based as far as they are applicable on those provisions of the Articles which govern decision-making by Directors (Articles 7 to 14).

6.2 The Directors may make rules of procedure for all or any committees, which prevail over rules derived from the Articles if they are not consistent with them.

## DECISION-MAKING BY DIRECTORS

**7. Directors to take decisions collectively**

7.1 The general rule about decision-making by Directors is that any decision of the Directors must be:

7.1.1 a decision at a meeting passed by a majority of the number of Directors appointed from time to time; or

7.1.2 a majority decision by a Directors' written resolution adopted in accordance with Article 8.

7.2 If, and for so long as, the Company has only one Director, the general rule does not apply, and the Director may take decisions without regard to any of the provisions of the Articles relating to Directors' decision-making (Articles 7 to 14).

## 8. Directors' written resolutions

8.1 Any Director may propose a Directors' written resolution and the company secretary (if any) must propose a Directors' written resolution if a Director so requests.

8.2 A Directors' written resolution is proposed by giving notice in writing of the proposed resolution to each Director.

8.3 A proposed Directors' written resolution is adopted when a majority of the Eligible Directors have signed one or more copies of it, provided that those Directors would have formed a quorum at a Directors' meeting had the resolution been proposed at such a meeting. Once a Directors' written resolution has been adopted, it must be treated as if it had been a decision taken at a Directors' meeting in accordance with the Articles.

8.4 An Alternate Director may sign a proposed Directors' written resolution (in addition to signing it in his capacity as a Director in his own right, if relevant) on behalf of each of his Appointors who:

8.4.1 have not signed or are not to sign the Directors' written resolution; and

8.4.2 are Eligible Directors in relation to the Directors' written resolution,

provided that (a) the Alternate Director is himself an Eligible Director in relation to the Directors' written resolution and (b) those persons actually signing the Directors' written resolution would have formed a quorum at a Directors' meeting had the resolution been proposed at such a meeting.

## 9. Calling a Directors' meeting

9.1 Any Director may call a Directors' meeting by giving notice of the meeting to the Directors or by authorising the company secretary (if any) to give such notice.

9.2 Notice of any Directors' meeting must indicate:

9.2.1 its proposed date and time;

9.2.2 where it is to take place; and

9.2.3 if it is anticipated that Directors participating in the meeting will not be in the same place, how it is proposed that they should communicate with each other during the meeting.

9.3 Notice of a Directors' meeting must be given to each Director. Notice does not need to be in writing. A Director who participates in a meeting shall be deemed to have received proper notice of the meeting.

## 10. Participation in Directors' meetings

10.1 Subject to the Articles, Directors participate in a Directors' meeting, or part of a Directors' meeting, when:

10.1.1 the meeting has been called and takes place in accordance with the Articles; and

10.1.2 they can each communicate to the others any information or opinions they have on any particular item of the business of the meeting.

10.2 In determining whether Directors are participating in a Directors' meeting, it is irrelevant where any Director is or how they communicate with each other.

10.3 If all the Directors participating in a meeting are not in the same place, they may decide that the meeting is to be treated as taking place wherever any of them is.

**11. Quorum for Directors' meetings**

11.1 The quorum for Directors' meetings is three Directors.

11.2 Subject to the Articles, a person who is an Alternate Director, but is not a Director in his own right, may be counted as participating for the purposes of determining whether a quorum is participating in any decision at a Directors' meeting, provided that his Appointor (or one of his Appointors):

11.2.1 is not participating in the decision at the Directors' meeting; and

11.2.2 would have been an Eligible Director in relation to the decision if he had been participating in it.

11.3 No Alternate Director may be counted as more than one Director for the purposes of determining whether a quorum is participating in any decision at a Directors' meeting.

**12. Chairing of Directors' meetings**

12.1 The Directors may appoint a Director to chair their meetings.

12.2 The person so appointed for the time being is known as the Chairman.

12.3 The Directors may terminate the Chairman's appointment at any time.

12.4 If the Directors have not appointed a Chairman, or if the Chairman is not participating in a Directors' meeting within 10 minutes of the time at which it was to start, the participating Directors must appoint one of themselves to chair it.

**13. Voting at Directors' meetings**

13.1 A decision is taken at a Directors' meeting by a majority of the votes of the Eligible Directors participating in the decision at the meeting.

13.2 Subject to the Articles, each Director participating in a decision at a Directors' meeting has one vote.

13.3 Subject to the Articles, an Alternate Director shall have one vote (in addition to his own vote in his capacity as a Director in his own right, if relevant) on any decision at a Directors' meeting for each of his Appointors who:

13.3.1 are not participating in the decision at the Directors' meeting; and

13.3.2 would have been Eligible Directors in relation to the decision if they had been participating in it.

13.4 If the numbers of votes for and against a proposal at a Directors' meeting are equal, the Chairman or other Director chairing the meeting shall not have a casting vote.

**14. Records of Directors' decisions to be kept**

The Directors must ensure that the Company keeps a record, in writing, for at least 10 years from the date of the decision recorded, of every majority decision taken by the Directors.

## DIRECTORS' INTERESTS

**15. Proposed transactions or arrangements with the Company**

15.1 If a Director is in any way, directly or indirectly, interested in a proposed transaction or arrangement with the Company, he must declare the nature and extent of that interest to the other Directors in accordance with this Article. Any declaration must be made before the Company enters into the transaction or arrangement. If a declaration of interest under this Article proves to be, or becomes, inaccurate or incomplete, a further declaration must be made. A declaration is not required if the Director is not aware of an interest or where the Director is not aware of the transaction or arrangement in question. For this purpose a Director is treated as being aware of matters of which he ought reasonably to be aware.

15.2 A Director need not declare an interest:

15.2.1 if it cannot reasonably be regarded as likely to give rise to a conflict of interest;

15.2.2 if, or to the extent that, the other directors are already aware of it (and for this purpose the other directors are treated as aware of anything of which they ought reasonably to be aware); or

15.2.3 if, or to the extent that, it concerns the terms of his service contract that have been or are to be considered:

15.2.3.1 by a meeting of the directors; or

15.2.3.2 by a committee of the Directors appointed for the purpose under these Articles.

**16. Existing transactions or arrangements with the Company**

16.1 If a Director is in any way, directly or indirectly, interested in a transaction or arrangement that has been entered into by the Company, he must declare the nature and extent of the interest to the other Directors in accordance with this Article. This Article does not apply if or to the extent of the interest has been declared under Clause 15.

16.2 The declaration must be made (a) at a meeting of the directors, or (b) by notice in writing or (c) by general notice. If a declaration of interest under this Article proves to be, or becomes, inaccurate or incomplete, a further declaration must be made. Any declaration must be made as soon as is reasonably practicable. This Article does not require a declaration of interest if which the Director is not aware or where the Director is not aware of the transaction or arrangement in question. For this purpose a Director is treated as being aware of matters of which he ought reasonably to be aware.

16.3 A Director need not declare an interest under this Article:

16.3.1 if it cannot reasonably be regarded as likely to give rise to a conflict of interest;

16.3.2 if, or to the extent that, the other Directors are already aware of it (and for this purpose the other Directors are treated as aware of anything of which they ought reasonably to be aware); or

16.3.3 if, or to the extent that, it concerns terms of his service contract that have been or are to be considered:

16.3.3.1 by a meeting of the Directors; or

16.3.3.2 by a committee of the Directors appointed for the purpose under these Articles.

**17. Director interest in transactions or arrangements with the Company**

17.1 Subject to compliance with these Articles, a Director may be a party to, or otherwise (directly or indirectly) interested in, any transaction or arrangement with the Company.

**18. Directors' conflicts of interest**

18.1 Provided that a Director has declared the nature and extent of his interest (other than a non-disclosable interest) to the other Directors, he shall be authorised:

18.1.1 to hold office as a Director or other officer of, be employed or engaged by, hold shares or other securities in, or otherwise be interested in, whether directly or indirectly, any group undertaking of the Company or any other undertaking in which the Company is otherwise (directly or indirectly) interested;

18.1.2 to participate in any scheme, transaction or arrangement for the benefit of employees or former employees of the Company or any group undertaking of the Company (including any pension fund or retirement, death or disability scheme or other bonus or employee benefit scheme);

18.1.3 to act as a trustee of any scheme for the benefit of employees or former employees of the Company or any group undertaking of the Company (including any pension, retirement, death or disability scheme or other bonus or employee benefit scheme);

18.1.4 to enter into, or otherwise be interested in, whether directly or indirectly, any transaction or arrangement in which the Company is (directly or indirectly) interested (other than a transaction or arrangement with the Company);

18.1.5 to be a party to any transaction or arrangement with any group undertaking of the Company or any other undertaking in which the Company is otherwise (directly or indirectly) interested; and

18.1.6 to be entitled to vote and count in the quorum at a meeting of directors or of a committee of the directors in respect of any decision in which he is interested.

A **"non- disclosable interest"** is an interest which cannot reasonably be regarded as likely to give rise to a conflict of interest or one that the other Directors are already aware of or ought reasonably to be aware of.

18.2 The following provisions of this Article apply to any authorisation of a matter by the Directors:

18.2.1 an authorisation may extend to any actual or potential conflict of interest (including a conflict of interest and duty and a conflict of duties) which may reasonably be expected to arise out of the matter so authorised;

18.2.2 an authorisation shall be subject to such conditions or limitations as the Directors may determine, whether at the time such authorisation is given or subsequently, and may be terminated by the Directors at any time; and

18.2.3 a Director must comply with any obligations imposed on him by the Directors pursuant to any authorisation.

18.3 If a matter, office, employment, engagement, position, transaction or arrangement or interest has been authorised either pursuant to Article 18.1, then the Director in question shall not be required to disclose to the Company any confidential information received by him (other than by virtue of his position as a Director) relating to such matter, office, employment, engagement, position, transaction or arrangement or interest, or to use such information in relation to the Company's affairs, if to do so would result in a breach of a duty or obligation of confidence owed by him in relation to or in connection with that matter, office, employment, engagement, position, transaction or arrangement or interest.

**19. Accounting for profit when interested**

19.1 Subject always to applicable law and the obligation of the Director to disclose his interest in proposed or existing transactions or arrangements with the Company in accordance with these Articles:

19.1.1 a Director shall not be accountable to the Company for any profit, remuneration or other benefit which he (or a person Connected with him) derives from or in connection with any interest (whether directly or indirectly) in any transaction or arrangement with the Company; and

19.1.2 no such transaction or arrangement shall be liable to be avoided on the grounds of any such interest, profit, remuneration or benefit.

19.2 Subject always to applicable law and the obligation of the Director to disclose his interest in accordance with Article 18.1 and to the terms on which any authorisation has been given:

19.2.1 a Director shall not be accountable to the Company for any profit, remuneration or other benefit which he (or a person connected with him) derives from or in connection with anything authorised pursuant to Article 18.1 or by the Directors; and

19.2.2 no such thing authorised shall be liable to be avoided on the grounds of any such interest, profit, remuneration or benefit.

**DIRECTORS' TERMS OF OFFICE**

**20. Methods of appointing Directors**

20.1 Any person who is willing to act as a Director, and is permitted by law to do so, may be appointed to be a Director:

20.1.1 by Ordinary Resolution; or

20.1.2 by a majority decision of the Directors.

**21. Termination of Director's appointment**

A person ceases to be a Director as soon as:

21.1 that person is removed as a Director:

21.1.1 by Ordinary Resolution; or

21.1.2 by a majority decision of the Directors, provided that any such removal shall be without prejudice to any claim such Director may have for breach of any contract of service between him and the Company;

21.2 that person ceases to be a Director by virtue of any provision of the Act or is prohibited from being a Director by law;

21.3 a bankruptcy order is made against that person;

21.4 a composition or arrangement is made with that person's creditors generally in satisfaction of that person's debts;

21.5 a registered medical practitioner who is treating that person gives a written opinion to the Company stating that that person has become physically or mentally incapable of acting as a Director and may remain so for more than three months; or

21.6 notice in writing is received by the Company from the Director that he is resigning from office, and such resignation has taken effect in accordance with its terms.

**22. Directors' remuneration**

22.1 Directors may undertake any services for the Company that the Directors decide.

22.2 Directors are entitled to such remuneration as the Directors determine:

22.2.1 for their services to the Company as Directors; and

22.2.2 for any other service which they undertake for the Company.

22.3 Subject to the Articles, a Director's remuneration may:

22.3.1 take any form; and

22.3.2 include any arrangements in connection with the payment of a pension, allowance or gratuity, or any death, sickness or disability benefits, to or in respect of that Director.

22.4 Unless the Directors decide otherwise, Directors' remuneration accrues from day to day.

22.5 An Alternate Director is not entitled to receive any remuneration from the Company for serving as an Alternate Director, except such part of his Appointor's remuneration as the Appointor may direct by notice in writing made to the Company.

**23. Directors' expenses**

The Company may pay any reasonable expenses which the Directors properly incur in connection with their attendance at:

23.1 meetings of Directors or committees of Directors; or

23.2 general meetings;

or otherwise in connection with the exercise of their powers and the discharge of their responsibilities in relation to the Company.

## ALTERNATE DIRECTORS

**24. Appointment and removal of Alternate Directors**

24.1 Any Director (other than an Alternate Director) (**"Appointor"**) may appoint as an alternate any person willing to act to:

24.1.1 exercise that Director's powers; and

24.1.2 carry out that Director's responsibilities,

in relation to the taking of decisions by the Directors in the absence of the alternate's Appointor, and may remove from office an alternate so appointed by him (an **"Alternate Director"**).

24.2 Any appointment or removal of an alternate must be effected by notice in writing to the Company signed by the Appointor, or in any other manner approved by the Directors. The appointment or removal shall take effect when the notice is received by the Company or on such later date (if any) specified in the notice.

24.3 The notice must:

24.3.1 identify the proposed or existing Alternate Director; and

24.3.2 in the case of a notice of appointment, contain (or be accompanied by) a statement signed by the proposed Alternate Director that the proposed Alternate Director is willing to act as the alternate of the Director giving the notice.

24.4 A person may act as an Alternate Director for more than one Director.

**25. Rights and responsibilities of Alternate Directors**

25.1 Except as the Articles specify otherwise, Alternate Directors:

25.1.1 are deemed for all purposes to be Directors;

25.1.2 are liable for their own acts and omissions;

25.1.3 are subject to the same restrictions as their Appointors; and

25.1.4 are not deemed to be agents of or for their Appointors.

**25.2** Subject to the Articles, an Alternate Director has the same rights in relation to any decision of the Directors and any meetings of committees of Directors as each of the alternate's Appointors. In particular, each Alternate Director is entitled to receive notice of all proposed Directors' written resolutions and of all Directors' meetings and meetings of committees of Directors which each of his Appointors is entitled to receive (disregarding, for these purposes, any absence of such Appointor from the United Kingdom), unless the Alternate Director is absent from the United Kingdom and has not given the Company an address to which such notices may be given by electronic means during his absence.

**26. Termination of Alternate Directorship**

An Alternate Director's appointment as an alternate for an Appointor terminates:

26.1 when that Appointor removes his Alternate Director in accordance with Article 24;

26.2 on the occurrence in relation to the Alternate Director of any event which, if it occurred in relation to that Appointor, would result in the termination of that Appointor's appointment as a Director;

26.3 on the death of that Appointor;

26.4 when that Appointor's appointment as a Director terminates; or

26.5 when notice in writing is received by the Company from the Alternate Director that he is resigning as an Alternate Director of that Appointor, and such resignation has taken effect in accordance with its terms.

## COMPANY SECRETARY

**27. Secretary's terms of office**

The Directors may appoint any person who is willing to act to be the company secretary for such term and on such conditions as they think fit, and may remove any company secretary so appointed.

## PART 3: SHARES AND DISTRIBUTIONS

## SHARES

**28. Powers to issue different classes of share**

28.1 Subject to the Articles, but without prejudice to the rights attached to any existing share, the Company may issue shares with such rights or restrictions as may be determined:

28.1.1 by Ordinary Resolution; or

28.1.2 if the Directors reasonably consider that the rights attaching to the Shares in issue at the time are not materially prejudiced or subordinated by the rights attaching the new shares, by a majority of the Directors or by a duly constituted committee of the board of Directors.

28.2 The Company may issue shares which are to be redeemed, or are liable to be redeemed at the option of the Company or the holder. The terms, conditions and manner of redemption of any such shares may be determined by the Directors and shall be set out in the Articles.

28.3 Subject to the Act, the Company may accept the surrender for no consideration of any paid up Share on such terms and in such manner as the Directors may determine.

**29. Rights of Pre-emption in favour of holders of C Shares**

29.1 Except for any Permitted Issue, each Qualifying C Holder (an "**Offeree**") shall be offered the same proportion of new equity shares (including warrants, options or other instruments convertible into or exchangeable for equity shares, or otherwise) ("**New Securities**") to be issued by the Company for cash as the proportion of Shares (of the Diluted Share Capital) held by such Offeree (as nearly as possible without involving fractions) at the same price and on the same terms and conditions as the Company proposes to offer New Securities to other third party investors (**"Pre-emptive Offer"**).

29.2 The Pre-emptive Offer shall:

29.2.1 be made by notice specifying the New Securities offered, the price for them, a time (being not later than 10 Business Days after receipt of the notice of the Pre-emptive Offer) within which the offer, if not accepted, shall be deemed to be declined and any other terms; and

29.2.2 invite each Offeree to state their acceptance of the number of any New Securities in excess of those offered to them (**"Extra Securities"**) that they wish to apply for.

29.3 Any New Securities not accepted (or deemed to be declined) under the Pre-emptive Offer (**"Declined Securities"**) shall be used to satisfy applications for Extra Securities. If there are insufficient Declined Securities to satisfy all such applications for Extra Securities, then such Declined Securities shall be allotted to the applicants of the Extra Securities (as nearly as possible without involving fractions) as follows:

29.3.1 pro rata to their holdings of C Shares immediately prior to the Pre-emptive Offer (as nearly as possible without increasing the number of Declined Securities allotted to any Shareholder beyond the number of Extra Securities applied for by them); and

29.3.2 then, any remaining Declined Securities to such applicants who have not yet been allotted the maximum number of Extra Securities applied for by them pro rata to their holdings of C Shares immediately prior to the Pre- emptive Offer (as nearly as possible without increasing the number of Declined Securities allotted to any Shareholder beyond the number of Extra Securities applied for by them). Any remaining Declined Securities shall continue to be allotted on the basis of this Article 29.3.2 until all Declined Securities have been allotted.

29.4 A Qualifying C Holder shall be entitled to transfer, by way of assignment, to its Affiliate or a Member of the same Fund Group, all or any of its rights under this Article 28.

## 30. Share certificates

30.1 The Company must issue each Member, free of charge, with one or more certificates in respect of the Shares which that Member holds if requested by such Member.

30.2 Every certificate must specify:

30.2.1 in respect of how many shares, of what class, it is issued;

30.2.2 the nominal value of those shares;

30.2.3 the amount paid up on them (including both the nominal value and any share premium); and

30.2.4 any distinguishing numbers assigned to them.

30.3 No certificate may be issued in respect of shares of more than one class.

30.4 If more than one person holds a share, only one certificate may be issued in respect of it.

## 31. Share transfers

31.1 No Member shall transfer any of its Shares, except in accordance with the terms of this Article 31 and Articles 31 to 34. The instrument of transfer of any Share shall be in any usual or common form or such other form as the Directors may determine.

31.2 Any Member may transfer any Shares (without restriction as to price or otherwise) to (a) an Affiliate of a Member; (b) the trustees for the time being of a Family Trust; (c) a Family Member provided that if the Family Member ceases to be a Family Member they shall, within 10 Business Days of so ceasing, transfer the Shares held by them to the original transferor and failing such transfer the Board may authorise any Director to execute and deliver the necessary transfer(s) as agent of the defaulting Member; (d) a Member of the same Fund Group; (e) any other Member; (f) any transferee of Shares, as provided for in Articles 31 or 33, or pursuant to the tag along rights provided in Articles 34 or 35; or (g) in respect of a particular proposed, transfer, a transferee approved by the Board, in their absolute discretion, (each of (a) to (g) being a **"Permitted Transferee"**).

31.3 The Board will authorise the registration of the transfer(s), and of the transferee(s) as the holder of the Shares so transferred, once (i) appropriate stamp duty (if any) has been paid, (ii) subject to the Member first providing to the Board with copies of the relevant trust documents forming the Family Trust permitted under these Articles, which identifies the trustees and beneficiaries of such Family Trust or, otherwise, demonstrating to the Company's reasonable satisfaction that the transferee is a Permitted Transferee; and (iii) subject to the proposed transferee having agreed to be bound by the Shareholders Agreement in all respects, in a form required by the Company.

31.4 Where Shares are held by trustees under a Family Trust:

31.4.1 those Shares may, on any change of trustees, be transferred to the new trustee(s) of that Family Trust;

31.4.2 those Shares may be transferred at any time to the settlor of that trust or any Family Member to whom that settlor could have transferred them under Article 31.2 if he had remained the holder of them; and

31.4.3 if any of those Shares cease to be held under a Family Trust other than in the circumstances set out in Article 31.4.2 above, or there cease to be any beneficiaries of the Family Trust other than a charity or charities, the trustees shall give a Transfer Notice within 10 Business Days in respect of all the Shares then held by those trustees and failing which the Board may authorise any Director to execute and deliver the necessary transfer(s) as agent of the defaulting Member. The Board will authorise the registration of the transfer(s), and of the transferee(s) as the holder of the Shares so transferred, once appropriate stamp duty (if any) has been paid.

31.5 If a Member transfers any to an Affiliate of such Member, if the Affiliate ceases to be an Affiliate it shall, within 10 Business Days of so ceasing, transfer the Shares held by them to the original transferor or an Affiliate of the original transferor and failing such transfer the Board may authorise any Director to execute and deliver the necessary transfer(s) as agent of the defaulting Member. The Board will authorise the registration of the transfer(s), and of the transferee(s) as the holder of the Shares so transferred, once appropriate stamp duty (if any) has been paid.

31.6 If a Member transfers to a Member of the same Fund Group (a " **Fund Transferee**"), if the Fund Transferee ceases to be a Member of the same Fund Group the Fund Transferee shall, within 5 Business Days of so ceasing, transfer the Shares held by it to the original transferor or a Member of the same Fund Group as the original transferor (without any restriction as to price or otherwise) and failing which, the Member shall be deemed to have delivered a Transfer Notice in respect of its Shares and the Board may authorise any Director to execute and deliver the necessary transfer(s) as agent of the defaulting Fund Transferee.

31.7 Notwithstanding any other provision of these Articles, no Share shall be transferred otherwise than pursuant to applicable laws, including US federal securities laws, as may be applicable to each relevant transfer of Shares and unless such sale is exempt from registration under the Securities Act and in compliance with all conditions on transfer imposed by any state "blue sky" or securities law and the Shareholders' Agreement.

## 32. Pre-emption rights on transfer

32.1 If at any time, any Member wishes to sell any of its Shares (the **"Seller"**) otherwise than to a Permitted Transferee), then such Seller shall give a notice in writing (the "**Transfer Notice**") to the Company. The Transfer Notice shall specify:

32.1.1 the Seller's desire to make such transfer;

32.1.2 the number of shares being offered for sale (the "**Transfer Shares**");

32.1.3 the price for which the Transfer Shares are to be sold (the "**Transfer Price**"); and

32.1.4 any other terms and conditions upon which the Seller proposes to sell the Transfer Shares.

32.2 Once a Transfer Notice has been given, it may not be revoked except with the prior written consent of the Board.

32.3 Upon receipt of the Transfer Notice, the Company shall have, within 30 days of receipt of the Transfer Notice (the "**First Offer Period"**), the right but not the obligation, to elect to purchase any or all of the Transfer Shares on the same terms and conditions as set forth in the Transfer Notice (**"Right of First Refusal"**), exercisable by confirmation in writing to the Seller of the total number of Transfer Shares that the Company would like to purchase on the terms of the Transfer Notice.

32.4 If the Company: (i) elects to purchase some but less than all of the Transfer Shares; (ii) elects not to purchase any Transfer Shares; (iii) fails to act within the First Offer Period; or (iv) is prohibited by the terms of any agreement or applicable law from exercising its Right of First Refusal, the Company shall notify each Qualifying C Holder within five days of: (x) the Company's determination to purchase less than all of the Transfer Shares; (y) the Company's determination not to purchase any of the Transfer Shares; or (z) following the expiration of the First Offer Period, of the same and specify the number of Transfer Shares remaining to be sold and the terms and conditions contained in the Transfer Notice ("**Second Transfer Notice**").

32.5 Upon receipt of the Second Transfer Notice, each Qualifying C Holder shall have, within 30 days of receipt of the Second Transfer Notice (the **"Second Offer Period"**), the right but not the obligation, to elect to purchase such proportion of the Transfer Shares set out in the Second Transfer Notice as the Shares held by such Qualifying C Holder (excluding the number of Transfer Shares), on the same terms and conditions as set forth in the Transfer Notice.

32.6 The Seller has 60 days from receipt of the last confirmation in writing from the Company of the identity of the proposed purchasers of the Transfer Shares, to sell to the Company and/or the relevant Qualifying C Holder, such number of Transfer Shares as specified in the written confirmation to the Seller from the Company. On receipt of payment for the Transfer Shares, the Seller shall deliver a stock transfer form to the purchaser of the relevant Transfer Shares, duly executed by the Seller, effecting a sale of the relevant Transfer Shares free and clear from any liens, charges or encumbrances.

32.7 After the expiry of the Second Offer Period, if: (i) all notices required to be given pursuant to Articles 31.1 and 31.4 have been duly given; and (ii) not all of the Transfer Shares have been purchased by the Company or by the Qualifying C Holders, the Seller shall have the right, for a period of 90 days from the earlier of:

32.7.1 the expiration of the Second Offer Period; or

32.7.2 written confirmation from the Company that no Qualifying C Holders will be purchasing any Transfer Shares, to sell to any third party the Transfer Shares at a price (and to the extent the Transfer Price contains any non-cash consideration, it shall be the same non-cash consideration and in the same proportion as was offered to the Company and/or Qualifying C Holders) not less that the Transfer Price and on the same terms and conditions as the Transfer Shares were offered to the Company and the Qualifying C Holders.

32.8 Should there be no sale to any third parties in accordance with Article 31.7, any subsequent proposed sale of the Transfer Shares must be offered to the Company and the Qualifying C Holders prior to any third party in accordance with the provisions of these Articles.

32.9 A Qualifying C Holder shall be entitled to transfer, by way of assignment, to its Affiliate or a Member of the same Fund Group, all or any of its rights under this Article 31.

**33. Drag-Along Rights**

33.1 Notwithstanding anything to the contrary in these Articles, in the event that certain Members wish to sell their Shares (the "**Drag Members**") to a bona fide arms' length purchaser (the "**Third Party Purchaser**") as part of an Approved Share Sale, the following shall apply:

33.1.1 the Drag Members shall have the right but not the obligation (the "**Drag Along Right**") to require all other Members (the "**Compelled Holders**") to accept in full the offer made to the Drag Members and sell their Shares to the Third Party Purchaser (or as the Third Party Purchaser shall direct) in accordance with the provisions of this Article 33;

33.1.2 the Drag Along Right may be exercised by the Drag Members serving notice to that effect (the "**Drag Along Notice**") on the Compelled Holders at any time which shall specify:

33.1.2.1 that the Compelled Holders are required to transfer all of their Shares (the "**Called Shares**");

33.1.2.2 the identity of the Third Party Purchaser and the identity of any person owning or controlling that third party; and

33.1.2.3 the consideration per Share for which the Compelled Members shall be obliged to sell, which shall be the same as that attributable by the offer from the Third Party Purchaser for each Share (subject to Article 32.5 below);

33.1.3 the only warranties that shall be given by the Compelled Holders will relate to title to their Called Shares and capacity to enter into the relevant documents and shall be given on a several basis subject to an aggregate liability cap of the consideration received by such Compelled Holder (save for in cases of fraud or willful misconduct);

33.1.4 the costs of the Members in respect of the transaction to sell to the Third Party Purchaser shall be borne by the Drag Members; and

33.1.5 the date on which the sale and purchase of Shares will be completed shall be the same date as the date proposed for completion of the sale of the Drag Members' Shares unless the Compelled Holders and the Drag Members agree otherwise.

33.2 A Drag Along Notice once given shall be irrevocable but shall lapse (and so shall the obligations under it) in the event that for any reason the Drag Members do not transfer their Shares which are the subject of the Approved Share Sale to the Third Party Purchaser within 40 Business Days of the date of the Drag Along Notice. The Drag Members shall be entitled to serve further Drag Along Notices following the lapse of any particular Drag Along Notice.

33.3 Each of the Compelled Holders shall be bound to accept the offer in the Drag Along Notice and will be deemed to have assumed such acceptance. In the event that any Compelled Holders fails to accept the offer made or, having accepted such offer, fails to complete the sale of any of his Called Shares or otherwise fails to take any action required of him under the terms of the offer, then the defaulting Compelled Holder shall be deemed to have irrevocably appointed any Director to be his agent to (i) execute all necessary transfer(s) on his behalf against receipt by the Company (on trust for such holder) of the purchase monies or any other consideration payable for the Called Shares; and (ii) deliver such transfer(s) to the Third Party Purchaser (or as they may direct), and the Directors shall register the Third Party Purchaser (or as they may direct) as the holder thereof. It shall be no impediment to registration of Shares under this Article 33.3 that no share certificate has been produced by any such defaulting Compelled Holder.

33.4 If, after any service of a Drag Along Notice, there becomes a new Member (which shall also include any person who acquires Shares which are issued or acquired on exercise of options granted under any option scheme (or otherwise) whether or not such exercise is made in contemplation of the offer or completion of the offer by the Third Party Purchaser) (a "**New Member**"), there shall be deemed to be served on such New Member a Drag Along Notice on the same terms as the previous Drag Along Notice. The New Member shall be bound to transfer all such Shares held by it to the Third Party Purchaser (or as directed by it) and the provisions of this Article 33 shall apply mutatis mutandis to the New Member except that completion of the sale of its Shares to the Third Party Purchaser shall be on the later of (a) the date the Drag Along Notice is deemed served on it or (b) the completion of the sale of all the Drag Members' Shares.

33.5 The amount of consideration payable by the Third Party Purchaser for each Called Share (the "**Drag Consideration**") shall be allocated between the Compelled Holders so as to ensure the order of application of the Payment Priority, and the directors shall not register any transfer of Shares if the Drag Consideration is not so distributed.

33.6 Notwithstanding anything to the contrary in these Articles, the rights of pre-emption on transfer set out in these Articles shall not apply to any acceptance of the offer by the Third Party Purchaser (including a sale pursuant to a Drag Along Notice).

**34. Tag Along Rights - A Shares**

34.1 Except in the case of a transfer to a Permitted Transferee pursuant to Article 31, and after going through the pre-emption procedure set out in Article 31, the provisions of this Article 34, shall apply if Kadmon and Kadmon's Affiliates, in aggregate hold more than 15 per cent of the Diluted Share Capital and in one or a series of related transactions, Kadmon proposes to transfer more than 25 per cent. of the aggregate number of A Shares held by Kadmon and Kadmon's Affiliates to a Third Party Purchaser (the "**Purchaser**"), before making such transfer procure that the proposed transferee of the A Shares makes an offer (a "**Tag Along Offer**") to all of the Athena Founders to purchase the same proportion of the A Shares held by each Athena Founder and their respective Permitted Transferees (**"Tag Member"**) as the proportion of Shares held being sold by Kadmon and its Affiliates (**"Tag Shares"**).

34.2 The Tag Along Offer shall set out:

34.2.1 the identity of the Purchaser;

34.2.2 the purchase price per Tag Share (the "**Tag Along Price**") including the calculation of any element not payable in cash and other terms and conditions of payment;

34.2.3 the proposed date of sale; and

34.2.4 the number of Tag Shares held by each Tag Member offered to be purchased in accordance with this Article 34.

34.3 Every Tag Member, on receipt of a Tag Along Offer, shall be bound within 20 Business Days of the date of such offer (which date shall be specified therein) ("**Tag Offer Period**") either to accept or reject such offer in writing (and in default of so doing shall be deemed to have rejected the offer). If a Tag Along Offer is not made Kadmon shall not be entitled to complete the proposed sale to the Purchaser and the Directors shall not register any transfer in respect of the proposed sale.

34.4 If the Tag Along Offer is accepted by any Tag Member within the Tag Offer Period, the completion of the proposed transfer shall be conditional upon the purchase of the Tag Shares on the terms and conditions as set out in the Tag Along Offer.

**35. Tag Along Rights - C Shares**

35.1 If one or more Members (**"Proposed Sellers"**) proposes to transfer (other than any permitted transfers in accordance with Article 30, and after going through the pre- emption procedure set out in Article 31) to any person (whether through a single transaction or a series of related transactions) such number of Shares which constitute 15 per cent or more of the Diluted Share Capital to a purchaser (together with its Connected Persons and any other persons with whom it is Acting in Concert) (together the **"Tag Buyer"**) (**"Proposed Sale"**), the Proposed Sellers shall not be entitled to transfer such Shares and no such Shares shall be capable of being purchased or transferred unless the Tag Buyer (or the Company in its capacity as agent for the Tag Buyer) shall have offered (**"Tag Offer"**) in accordance with this Article 35 to purchase from each holder of C Shares (not being a Tag Buyer) (**"Other Shareholders"**) such proportion of the number of each class of Shares registered in their name (**"Tagged Shares"**) as is equal to the proportion which the Shares that the Proposed Sellers are proposing to transfer to the Tag Buyer bears to the Proposed Sellers' total holding of A Shares that would be deemed to be held by the Proposed Seller on the date of such Proposed Sale, if all C Shares were converted and reclassified as A Shares by applying the Conversion Rate applicable on such date in accordance with these Articles.

35.2 A Tag Offer shall be made by notice specifying:

35.2.1 the identity of the Tag Buyer;

35.2.2 the number of Shares of each class that the Proposed Sellers are proposing to transfer to the Tag Buyer and the proportion that this bears (on a, as converted basis, as referred to in Article 35.1 above) to the Proposed Seller's total holding of Shares and the number of Shares of each class that the Tag Buyer is therefore offering to purchase from the relevant Other Shareholder;

35.2.3 the amount and form of consideration and the proportion of cash and/or securities that the Tag Buyer is proposing to pay for each of those Shares (determined in accordance with Article 35.3);

35.2.4 the proposed, place, date and time of transfer;

35.2.5 a time (being not less than 20 Business Days) within which the Tag Offer, if not accepted, shall be deemed to be declined; and

35.2.6 to the extent not set out in the accompanying documents, any other terms and conditions of sale on which the Tag Buyer is proposing to purchase the Proposed Sellers and the Other Shareholder's Shares,

and shall be accompanied by all documents required to be executed by the Other Shareholders if they accept the Tag Offer.

35.3 The amount and form of consideration and the proportion of cash and/or securities which the Tag Buyer shall offer and is proposing to pay for each of the Tagged Shares shall be the same as that offered and to be paid for each of the Proposed Seller's Shares being transferred to the Tag Buyer pursuant to the Proposed Sale provided always that if the Proposed Sale does not include Shares in the same class as any Tagged Share, by deriving the value of each other class of Tagged Share by reference to the consideration payable for each Tagged Share, as adjusted by the number of Shares of such class as would arise from application of the Conversion Rights on the date of the Tag Offer in accordance with these Articles.

35.4 Each Other Shareholder who accepts the Tag Offer within the offer period (**"Accepting Shareholder"**) shall be required to:

35.4.1 transfer the legal and beneficial title to all of their Tagged Shares to the Tag Buyer free from all liens, charges and encumbrances and together with all rights attaching to them and with full title guarantee;

35.4.2 subject to Article 35.3, sell their Tagged Shares on the same terms and conditions (including the same representations, warranties, covenants, undertakings, indemnities and requirements relating to contributing to any retention on a pro rata basis) as are to be given to and by the Proposed Sellers pursuant to the Proposed Sale;

35.4.3 deliver to the Tag Buyer the share certificates for their Tagged Shares (or an indemnity in a form reasonably satisfactory to the Directors for lost certificates) and a duly executed sale agreement (in a form agreed by the Proposed Sellers) setting out the relevant terms and conditions of sale; and

35.4.4 pay their proportionate share of such fees, costs and expenses that are to be borne by the Accepting Shareholders pursuant to Article 35.7.

35.5 Completion of the sale and purchase of any Tagged Shares in respect of which the Tag Offer has been accepted shall be conditional upon, and shall take place on the same date and at the same time and place as, the completion of the Proposed Sale (unless any of the Accepting Shareholders and the Tag Buyer agree otherwise), save that if any Accepting Shareholder fails to comply with their obligations under Article 35.4 on or before the completion of the Proposed Sale:

35.5.1 the completion of the Proposed Sale may be made without the completion of the sale and purchase of that Accepting Shareholder's Tagged Shares (provided that it shall be on no more favourable terms and conditions to the Proposed Sellers than those stated in the original Tag Offer); and

35.5.2 the Tag Buyer shall not be under any further obligation to purchase those Tagged Shares.

35.6 If some or all of the Other Shareholders do not accept the Tag Offer within the offer period, the completion of the Proposed Sale may be made within three months of the end of that period (provided that it shall be on no more favourable terms and conditions to the Proposed Sellers than those stated in the original Tag Offer).

35.7 The reasonable transaction fees, costs and expenses incurred by the Proposed Sellers and the Accepting Shareholders that are attributable to the transfer of Shares made in accordance with this Article 35 shall be borne by each of the Proposed Sellers and the Accepting Shareholders pro rata to their holdings of Shares being transferred.

**36. Share Rights - Return of Capital**

36.1 On a return of capital on liquidation, deemed liquidation event, winding- up or otherwise (excluding, for the avoidance of doubt, a conversion, redemption, purchase of shares or capital reduction), the surplus assets and retained profits of the Company available for distribution among the holders of Shares (after payment of the Company's liabilities) shall be applied in the following manner and order of priority (the "**Payment Priority**"):

36.1.1 firstly in paying to the holders of C Shares, a sum equal to the C Share Starting Price in respect of such shares; and

36.1.2 secondly, the balance of such assets (if any) shall be distributed amongst the holders of A Shares pro rata to the number of Shares held by each of them respectively.

36.2 All arrears and/or accruals of dividends must be cleared prior to the distribution of assets pursuant to this Article 35.

**37. Share Rights - Voting**

37.1 The Shares shall confer on each holder of Shares the right to receive notice of and to attend, speak and vote at all general meetings of the Company and to receive and vote on proposed written resolutions of the Company.

37.2 On a show of hands each holder of Shares who (being an individual) is present in person or by proxy or (being a corporation) is present by a duly authorised representative or by proxy shall have one vote and on a poll or a written resolution each such holder so present shall have one vote for each Share held by him.

37.3 No voting rights attached to a Share which is nil paid may be exercised:

37.3.1 at any general meeting, at any adjournment of it or at any poll called at or in relation to it; or

37.3.2 on any proposed written resolution, until all of the amounts payable to the Company in respect of that Share have been paid.

**38. Exit Provisions**

38.1 Unless waived by the holders of at least 50.5% of the C Shares then in issue, on a Sale, the Proceeds of Sale received or receivable by Members at any time in respect of the Shares that are the subject of the Sale shall be reallocated between them so as to ensure the order of application of the aggregate Proceeds of Sale shall be in the same order of application as the Payment Priority as if the date of such Sale were the date of the return of capital under Article 35 and as if the Proceeds of Sale represented all of the assets of the Company available for distribution to the Members and the Directors shall not register any transfer of Shares if the Proceeds of Sale are not so distributed save in respect of any Shares not sold in connection with that Sale, provided that if the Proceeds of Sale are not settled in their entirety upon completion of the Sale:

38.1.1 the Directors shall not be prohibited from registering the transfer of the relevant Shares so long as the Proceeds of Sale that are settled have been distributed in accordance with the Payment Priority; and

38.1.2 the members shall take any action required by the holders of C Shares to ensure that the Proceeds of Sale in their entirety are distributed in accordance with the Payment Priority.

38.2 In the event that the Proceeds of Sale are distributed on more than one occasion (for any deferred or contingent consideration or otherwise), the consideration so distributed on any further occasion shall be paid by continuing the distribution from the previous distribution of consideration in accordance with the Payment Priority.

38.3 On an Asset Sale, the surplus assets of the Company remaining after payment of the Company's liabilities shall be distributed (to the extent the Company is lawfully permitted to do so) in accordance with the Payment Priority provided always that if it is not lawful for the Company to distribute its surplus assets in accordance with the provisions of these Articles, the Members shall take any action required by the Board including, but without prejudice to the generality of this Article 37, actions that may be necessary to put the Company into voluntary liquidation so that Article 35 applies.

38.4 On an Exit, all shareholders shall take all action necessary in connection with the Exit, including, but not limited to: (i) voting to approve the terms of the Exit and any ancillary matters as may be necessary in the board's opinion to effect such; and (ii) (to the extent applicable) waiving any pre-emption or consent rights, or other restrictions on the transfer of such shareholders' shares. If a Member fails to comply with the provisions of this Article, the Company shall be constituted as the agent of each such defaulting Member for taking such actions as are necessary to effect the Exit and the Directors may be authorised to execute and deliver on behalf of such defaulting Member the necessary documents and the Company may receive any consideration due to the defaulting Member in trust for such defaulting Member.

**39. Conversion of C Shares**

39.1 A member holding C Shares may, by service of a written notice served at any time to the Company's registered office, require the conversion and reclassification of all C Shares held by such member to A Shares, at the Conversion Rate and such conversion and reclassification shall occur automatically on the date of such notice.

39.2 All C Shares in issue shall automatically be converted and reclassified as A Shares with effect from and immediately prior to (and conditional upon) a Qualified IPO being effected, at the Conversion Rate. If such Qualified IPO does not take effect, such conversion shall be deemed not to have occurred.

39.3 In the case of Article 40.1 not more than five Business Days after the written notice and in the case of Article 40.2, at least five Business Days prior to the occurrence of the Qualified IPO, each relevant C Share holder shall deliver the certificate (or an indemnity in a form reasonably satisfactory to the Board in respect of any lost certificate) in respect of the C Share being converted to the Company at its registered office.

39.4 Following the conversion in accordance with this Article 40, the Company shall enter the holder of the converted C Shares on the register of members of the Company as the holder of the appropriate number of A Shares.

39.5 The Directors may effect such conversion in any manner available under applicable law, including redeeming or repurchasing the relevant C Shares and applying the proceeds thereof towards payment for the new A Shares. For purposes of the redemption or repurchase, the Directors may, subject to the Company being able to pay its debts in the ordinary course of business, make payments out of amounts standing to the credit of the Company's share premium account or out of its capital.

## 40. Variation of Class Rights

40.1 The A Shares and the C Shares shall rank *pari passu* and, except where otherwise provided in these Articles, shall entitle the holders thereof to the same rights and privileges.

40.2 Any special rights attaching to the C Shares may be varied or abrogated by the consent in writing of the holders of a majority of the C Shares.

40.3 Except as provided in Article 41.2 with respect to C Shares, whenever the capital of the Company is divided into different Classes (and as otherwise determined by the Directors) the rights attached to any such Class may, subject to any rights or restrictions for the time being attached to any Class only be varied with the consent in writing of the holders of not less than 75% of the issued Shares of the relevant Class, or with the sanction of a resolution passed at a separate meeting of the holders of the Shares of such Class by a majority of 75% of the votes cast at such a meeting. To every such separate meeting all the provisions of these Articles relating to general meetings of the Company or to the proceedings thereat shall, mutatis mutandis, apply, except that the necessary quorum shall be one or more Persons at least holding or representing by proxy one-third in nominal or par value amount of the issued Shares of the relevant Class (but so that if at any adjourned meeting of such holders a quorum as above defined is not present, those Shareholders who are present shall form a quorum) and that, subject to any rights or restrictions for the time being attached to the Shares of that Class, every Shareholder of the Class shall on a poll have one vote for each Share of the Class held by him. The holders of not less than 15% of the issued Shares of that Class (being persons who did not consent to or vote in favour of the resolution to vary the rights attached to the Class) may apply to the court to have such variation cancelled.

40.4 The rights conferred upon the holders of the Shares of any Class issued with preferred or other rights shall not, subject to any rights or restrictions for the time being attached to the Shares of that Class, be deemed to be varied by, inter alia, the creation, allotment or issue of further Shares ranking pari passu with or subsequent to them or the redemption or purchase of any Shares of any Class by the Company.

**DIVIDENDS AND OTHER DISTRIBUTIONS**

## 41. Payment of dividends

41.1 Any profits lawfully available for distribution and which the Company determines to distribute in respect of any financial year shall be distributed to the holders of the Shares.

41.2 Dividends shall be paid in cash net of tax and shall be distributed to the Members (as relevant) pro rata to the number of Shares held by each such holder, respectively.

41.3 All arrears and/or accruals of dividends must be cleared prior to the distribution of assets pursuant to this Article 41.3.

**PART 4: DECISION-MAKING BY MEMBERS**

**WRITTEN RESOLUTIONS**

## 42. Written resolutions

A resolution of the Members (or a class of Members) may be passed as a written resolution in accordance with these Articles. A resolution in writing signed by all the Members for the time being entitled to receive notice of and to attend and vote at general meetings of the Company (or being corporations by their duly authorised representatives) shall be as valid and effective as if the same had been passed at a general meeting of the Company duly convened and held.

## GENERAL MEETINGS

## ORGANISATION OF GENERAL MEETINGS

**43. Calling general meetings**

43.1 Any Director of the Company may call a general meeting.

43.2 If, and for so long as, the Company has only a single Member, such Member shall be entitled at any time to call a general meeting.

43.3 A Member present in person or by proxy at a general meeting shall be deemed to have received proper notice of the meeting and, if required, of the purposes for which it was called.

**44. Quorum for general meetings**

No business other than the appointment of the Chairman of the meeting is to be transacted at a general meeting if the persons attending it do not constitute a quorum. The quorum for meetings of the Members shall be two persons entitled to vote upon the business to be transacted each being a Member or a proxy for a Member or a duly authorised representative of a corporation.

**45. Chairing general meetings**

45.1 If the Directors have appointed a Chairman, the Chairman shall chair general meetings if present and willing to do so.

45.2 If the Directors have not appointed a Chairman, or if the Chairman is unwilling to chair the general meeting or is not present within 10 minutes of the time at which a meeting was due to start:

45.2.1 the Directors present; or

45.2.2 (if no Directors are present within 10 minutes of the time at which the meeting was due to start) the Members present at the meeting,

must appoint a Director or Member to chair the meeting, and the appointment of the Chairman of the meeting must be the first business of the meeting.

**46. Adjournment**

46.1 If the persons attending a general meeting within half an hour of the time at which the meeting was due to start do not constitute a quorum, or if during a meeting a quorum ceases to be present, the Chairman of the meeting must adjourn it. If at such an adjourned meeting the persons attending within half an hour of the time at which the meeting was due to start do not constitute a quorum, or if during such an adjourned meeting a quorum ceases to be present, the meeting shall be dissolved.

46.2 The Chairman of the meeting may adjourn a general meeting at which a quorum is present if:

46.2.1 the meeting consents to an adjournment; or

46.2.2 it appears to the Chairman of the meeting that an adjournment is necessary to protect the safety of any person attending the meeting or ensure that the business of the meeting is conducted in an orderly manner.

46.3 The Chairman of the meeting must adjourn a general meeting if directed to do so by the meeting.

46.4 When adjourning a general meeting, the Chairman of the meeting must:

46.4.1 either specify the time and place to which it is adjourned or state that it is to continue at a time and place to be fixed by the Directors; and

46.4.2 have regard to any directions as to the time and place of any adjournment which have been given by the meeting.

46.5 If the continuation of an adjourned meeting is to take place more than 14 days after it was adjourned, the Company must give at least seven clear days' notice of it (that is, excluding the day on which the notice is given and the day of the adjourned meeting):

46.5.1 to the same persons to whom notice of the Company's general meetings is required to be given; and

46.5.2 in the same manner in which such notice is required to be given and containing the same information which such notice is required to contain.

## VOTING AT GENERAL MEETINGS

**47. Voting: general**

A resolution put to the vote of a general meeting must be decided by way of a poll in accordance with these Articles.

**48. Poll votes**

48.1 Polls must be taken in such manner as the Chairman of the meeting directs.

**49. Content of Proxy Notices**

49.1 Proxies may only validly be appointed by a notice in writing (**"Proxy Notice"**) which:

49.1.1 states the name and address of the Member appointing the proxy;

49.1.2 identifies the person appointed to be that Member's proxy and the general meeting or adjourned meeting in relation to which that person is appointed;

49.1.3 is signed by or on behalf of the Member appointing the proxy, or is authenticated in such manner as the Directors may otherwise determine;

49.1.4 is delivered to the Company in accordance with the Articles and any instructions contained in the notice of the general meeting or adjourned meeting to which it relates; and

49.1.5 is received by the Company no later than 48 hours (excluding any part of a day that is not a Business Day) before the time appointed for the commencement of the general meeting or adjourned meeting to which the Proxy Notice relates or such later time as the Directors may determine.

49.2 The Company may require Proxy Notices to be delivered in a particular form, and may specify different forms for different purposes.

49.3 Proxy Notices may specify how the proxy appointed under them is to vote (or that the proxy is to abstain from voting) on one or more resolutions.

49.4 Unless a Proxy Notice indicates otherwise, it must be treated as:

49.4.1 allowing the person appointed under it as a proxy discretion as to how to vote on any ancillary or procedural resolutions put to the meeting; and

49.4.2 appointing that person as a proxy in relation to any adjournment of the general meeting to which it relates as well as the meeting itself.

**50. Delivery of Proxy Notices**

50.1 A person who is entitled to attend, speak or vote on a poll at a general meeting remains so entitled in respect of that meeting or any adjournment of it, even though a valid Proxy Notice has been delivered to the Company by or on behalf of that person. However, if that person votes at the meeting or adjourned meeting on a resolution, then as regards that resolution any Proxy Notice delivered to the Company by or on behalf of that person shall, on a poll, be invalid to the extent that such person votes in respect of the shares to which the Proxy Notice relates.

50.2 An appointment under a Proxy Notice may be revoked by delivering to the Company a notice in writing given by or on behalf of the person by whom or on whose behalf the Proxy Notice was given.

50.3 A notice revoking a proxy appointment only takes effect if it is received by the Company before the commencement of the meeting or adjourned meeting to which it relates.

50.4 If a Proxy Notice is not executed by the person appointing the proxy, it must be accompanied by written evidence of the authority of the person who executed it to execute it on the Appointor’s behalf.

50.5 When two or more valid but different Proxy Notices are received in respect of the same share for use at the same meeting or adjourned meeting, the one which is last validly received (regardless of its date or the date of its execution) shall be treated as replacing and revoking the other(s) as regards that share. If the Company is unable to determine which was last received, none of them shall be treated as valid in respect of that share.

**51. Corporate representatives**

Where a Member that is a corporation has authorised a representative or representatives to act on its behalf at a general meeting:

51.1 the corporation shall, for the purposes of these Articles, be deemed to be present in person at any such meeting if any such representative is present at it, and all references to attendance and voting in person shall be construed accordingly;

51.2 a Director or the company secretary (if any) may require any such representative to produce a certified copy of such authority before such representative is entitled to exercise any power on behalf of the corporation which he represents; and

51.3 a vote given by such representative at a general meeting or adjourned meeting shall be valid even though his authority has previously terminated unless notice in writing of the termination was received by the Company before the commencement of that meeting.

**52. Amendments to resolutions**

52.1 An Ordinary Resolution to be proposed at a general meeting may be amended by Ordinary Resolution if:

52.1.1 notice of the proposed amendment is given to the Company in writing by a person entitled to vote at the general meeting at which it is to be proposed not less than 48 hours before the meeting is to take place (or such later time as the Chairman of the meeting may determine); and

52.1.2 the proposed amendment does not, in the reasonable opinion of the Chairman of the meeting, materially alter the scope of the resolution.

52.2 A Special Resolution to be proposed at a general meeting may be amended by Ordinary Resolution, if:

52.2.1 the Chairman of the meeting proposes the amendment at the general meeting at which the resolution is to be proposed; and

52.2.2 the amendment does not go beyond what is necessary to correct a grammatical or other non-substantive error in the resolution.

52.3 If the Chairman of the meeting, acting in good faith, wrongly decides that an amendment to a resolution is out of order, the Chairman's error does not invalidate the vote on that resolution.

## PART 5: ADMINISTRATIVE ARRANGEMENTS

### 53. Form of notice

Any notice or other document to be given pursuant to the Articles (other than a notice calling a meeting of the Directors) must be in writing.

### 54. Notices to the Company

Any notice, document or other information may be served on or sent or supplied to the Company by anyone:

54.1 by sending it through the post in a prepaid envelope addressed to the Company or any officer of the Company at its registered office or such place in the United Kingdom as may from time to time be specified by the Company for that purpose;

54.2 by delivering it by hand to or leaving it at its registered office or such place in the United Kingdom as may from time to time be specified by the Company for that purpose in an envelope addressed to the Company or any officer of the Company;

54.3 by sending or supplying it by electronic means to an address specified by the Company from time to time for that purpose; or

54.4 by any other means authorised in writing by the Company.

### 55. Notices to Members

55.1 Any notice, document or other information may be served on or sent or supplied to any Member:

55.1.1 personally;

55.1.2 by sending it through the post in a prepaid envelope addressed to the Member at his registered address;

55.1.3 by delivering it by hand to or leaving it at that address in an envelope addressed to the Member;

55.1.4 by sending or supplying it by electronic means to an address notified by the Member to the Company from time to time for that purpose; or

55.1.5 by any other means authorised in writing by the relevant Member.

55.2 Nothing in Article 55.1 shall affect any provision of the Act requiring offers, notices or documents to be served on or sent or supplied to a Member in a particular way.

## 56. Notices to Directors

Any notice, document or other information may be served on or sent or supplied to a Director by the Company or by any other Director or the company secretary (if any):

56.1 personally;

56.2 (other than a notice of a proposed Directors' written resolution) by word of mouth;

56.3 by sending it through the post in a prepaid envelope addressed to the Director at his registered address or such other postal address as may from time to time be specified by him for that purpose;

56.4 by delivering it by hand to or leaving it at that address in an envelope addressed to him;

56.5 by sending or supplying it by electronic means to an address specified from time to time by the Director for that purpose; or

56.6 by any other means authorised in writing by the Director.

## 57. Service of notices on Members or Directors

Any notice, document or other information (other than any notice, document or other information given to the Company including, for the avoidance of doubt, the appointment of a proxy):

57.1 addressed to a Member or a Director in the manner prescribed by the Articles shall, if sent by post (whether in hard copy or electronic form), be deemed to have been received:

57.1.1 (if prepaid as first class) 24 hours after it was posted;

57.1.2 (if prepaid as second class) 48 hours after it was posted;

57.1.3 (if prepaid as airmail) 72 hours after it was posted,

and, in proving such receipt, it shall be sufficient to prove that the envelope containing such notice, document or other information was properly addressed, prepaid and put in the post;

57.2 not sent by post, but addressed to a Member or a Director and delivered by hand to or left at an address in accordance with the Articles, shall be deemed to have been received on the day it was so delivered or left;

57.3 served, sent or supplied to a Member or a Director by electronic means shall be deemed to have been received on the day it was sent, and, in proving such receipt, it shall be sufficient to show that such notice, document or information was properly addressed;

57.4 served, sent or supplied by any other means authorised in writing by the Member or the Director shall be deemed to have been received when the Company has carried out the action it has been authorised to take for that purpose.

## 58. Right to inspect accounts and other records

All books and records of the Company shall be maintained at the Company's principal place of business, and each Member, and the Member's duly authorised representative, shall have access to them at such office of the Company and the right to inspect and copy them at reasonable times for any purpose reasonably related to its interest in the Company.

### DIRECTORS' INDEMNITY AND INSURANCE

## 59. Indemnity

59.1 Subject to Article 58.2, but without prejudice to any indemnity to which a relevant officer is otherwise entitled:

59.1.1 each relevant officer shall be indemnified out of the Company's assets against all costs, charges, losses, expenses and liabilities incurred by him as a relevant officer:

59.1.1.1 in the actual or purported execution and/or discharge of his duties, or in relation to them; and

59.1.1.2 in relation to the Company's (or any associated company's) activities as trustee of an occupational pension scheme (as defined in section 235(6) of the UK Companies Act 2006),

including (in each case) any liability incurred by him in defending any civil or criminal proceedings, in which judgment is given in his favour or in which he is acquitted or the proceedings are otherwise disposed of without any finding or admission of any material breach of duty on his part or in connection with any application in which the court grants him, in his capacity as a relevant officer, relief from liability for negligence, default, breach of duty or breach of trust in relation to the Company's (or any associated company's) affairs; and

59.1.2 the Company may provide any relevant officer with funds to meet expenditure incurred or to be incurred by him in connection with any proceedings or application referred to in Article 58.1.1 and otherwise may take any action to enable any such relevant officer to avoid incurring such expenditure.

59.2 This Article 58 does not authorise any indemnity which would be prohibited or rendered void by any provision of applicable law.

59.3 In this Article 58:

59.3.1 companies are associated if one is a subsidiary of the other or both are subsidiaries of the same body corporate; and

59.3.2 a "**relevant officer**" means any Director or other officer or former director or other officer of the Company or an associated company (including any company which is a trustee of an occupational pension scheme (as defined by section 235(6) of the UK Companies Act 2006.

## 60. Insurance

60.1 The Directors may decide to purchase and maintain insurance, at the expense of the Company, for the benefit of any relevant officer in respect of any relevant loss.

60.2 In this Article 59:

60.2.1 a “**relevant officer**” means any Director or other officer or former director or other officer of the Company or an associated company (including any such company which is a trustee of an occupational pension scheme as defined by section 235(6) UK Companies Act 2006);

60.2.2 a “**relevant loss**” means any loss or liability which has been or may be incurred by a relevant officer in connection with that relevant officer’s duties or powers in relation to the Company, any associated company or any pension fund or employees’ share scheme of the Company or associated company; and

60.2.3 companies are associated if one is a subsidiary of the other or both are subsidiaries of the same body corporate.

## ALTERATION OF SHARE CAPITAL

**61. Alternation of share capital**

61.1 The Company may from time to time by Ordinary Resolution increase the share capital by such sum, to be divided into Shares of such classes and amount, as the resolution shall prescribe.

61.2 The Company may by Ordinary Resolution:

61.2.1 consolidate and divide all or any of its share capital into Shares of a larger amount than its existing Shares; and

61.2.2 convert all or any of its paid up Shares into stock and reconvert that stock into paid up Shares of any denomination.

The Company may by Special Resolution reduce its share capital and any capital redemption reserve in any manner authorised by law.

**THE COMPANIES LAW (AS AMENDED)**

**COMPANY LIMITED BY SHARES**

**AMENDED AND RESTATED**

**MEMORANDUM OF ASSOCIATION**

**OF**

**MEIRAGTX HOLDINGS PLC**

**(ADOPTED BY SPECIAL RESOLUTION DATED ______2018)**

WALKERS

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**REF: CM/SP/M6113-151627**

**THE COMPANIES LAW (AS AMENDED)**

**COMPANY LIMITED BY SHARES**

**AMENDED AND RESTATED**

**MEMORANDUM OF ASSOCIATION**

**OF**

**MEIRAGTX HOLDINGS PLC**

**(ADOPTED BY SPECIAL RESOLUTION DATED _______ 2018)**

1. The name of the company is MeiraGTx Holdings plc (the "**Company**").

2. The registered office of the Company will be situated at the offices of Walkers Corporate Limited, Cayman Corporate Centre, 27 Hospital Road, George Town, Grand Cayman KY1-9008, Cayman Islands or at such other location as the Directors may from time to time determine.

3. The objects for which the Company is established are unrestricted and the Company shall have full power and authority to carry out any object not prohibited by any law as provided by Section 7(4) of the Companies Law (as amended) of the Cayman Islands (the "**Companies Law**").

4. The Company shall have and be capable of exercising all the functions of a natural person of full capacity irrespective of any question of corporate benefit as provided by Section 27(2) of the Companies Law.

5. The Company will not trade in the Cayman Islands with any person, firm or corporation except in furtherance of the business of the Company carried on outside the Cayman Islands; provided that nothing in this section shall be construed as to prevent the Company effecting and concluding contracts in the Cayman Islands, and exercising in the Cayman Islands all of its powers necessary for the carrying on of its business outside the Cayman Islands.

6. The liability of the shareholders of the Company is limited to the amount, if any, unpaid on the shares respectively held by them.

7. The capital of the Company is **US$50,000** divided into **1,288,327,750** shares with a nominal or par value of **US$0.00003881** provided always that subject to the Companies Law and the Articles of Association the Company shall have power to redeem or purchase any of its shares and to sub-divide or consolidate the said shares or any of them and to issue all or any part of its capital whether original, redeemed, increased or reduced with or without any preference, priority, special privilege or other rights or subject to any postponement of rights or to any conditions or restrictions whatsoever and so that unless the conditions of issue shall otherwise expressly provide every issue of shares whether stated to be ordinary, preference or otherwise shall be subject to the powers on the part of the Company hereinbefore provided.

8. The Company may exercise the power contained in Section 206 of the Companies Law to deregister in the Cayman Islands and be registered by way of continuation in some other jurisdiction.

**THE COMPANIES LAW (AS AMENDED)**

**COMPANY LIMITED BY SHARES**

**AMENDED AND RESTATED**

**ARTICLES OF ASSOCIATION**

**OF**

**MEIRAGTX HOLDINGS PLC**

**(ADOPTED BY SPECIAL RESOLUTION DATED _____________ 2018)**

WALKERS

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**REF: CM/SP/M6113-151627**

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**OF**

**MEIRAGTX HOLDINGS PLC**

**(ADOPTED BY SPECIAL RESOLUTION DATED ______2018)**

## TABLE A

The Regulations contained or incorporated in Table 'A' in the First Schedule of the Companies Law shall not apply to MeiraGTx Holdings plc (the "**Company**") and the following Articles shall comprise the Articles of Association of the Company.

## INTERPRETATION

1. In these Articles the following defined terms will have the meanings ascribed to them, if not inconsistent with the subject or context:

"**Articles**" means these articles of association of the Company, as amended or substituted from time to time.

"**Branch Register**" means any branch Register of such category or categories of Members as the Company may from time to time determine.

"**Class**" or "**Classes**" means any class or classes of Shares as may from time to time be issued by the Company.

"**Commission**" means the Securities and Exchange Commission of the United States of America or any other federal agency for the time being administering the Securities Act.

"**Companies Law**" means the Companies Law (as amended) of the Cayman Islands.

"**Designated Stock Exchange**" means any national securities exchange or automated quotation system on which the Company's securities are then traded, including but not limited to the New York Stock Exchange and Nasdaq Stock Market.

"**Directors**" means the directors of the Company for the time being, or as the case may be, the directors assembled as a board or as a committee thereof.

"**Memorandum of Association**" means the memorandum of association of the Company, as amended or substituted from time to time.

"**Office**" means the registered office of the Company as required by the Companies Law.

"**Officers**" means the officers for the time being and from time to time of the Company.

"**Ordinary Resolution**" means a resolution:

(a) passed by a simple majority of such Shareholders as, being entitled to do so, vote in person or, where proxies are allowed, by proxy at a general meeting of the Company and where a poll is taken regard shall be had in computing a majority to the number of votes to which each Shareholder is entitled; or

(b) approved in writing by all of the Shareholders entitled to vote at a general meeting of the Company in one or more instruments each signed by one or more of the Shareholders and the effective date of the resolution so adopted shall be the date on which the instrument, or the last of such instruments, if more than one, is executed.

"**paid up**" means paid up as to the par value in respect of the issue of any Shares and includes credited as paid up.

"**Person**" means any natural person, firm, company, joint venture, partnership, corporation, association or other entity (whether or not having a separate legal personality) or any of them as the context so requires, other than in respect of a Director or Officer in which circumstances Person shall mean any person or entity permitted to act as such in accordance with the laws of the Cayman Islands.

"**Principal Register**", where the Company has established one or more Branch Registers pursuant to the Companies Law and these Articles, means the Register maintained by the Company pursuant to the Companies Law and these Articles that is not designated by the Directors as a Branch Register.

"**Register**" means the register of Members of the Company required to be kept pursuant to the Companies Law and includes any Branch Register(s) established by the Company in accordance with the Companies Law.

"**Seal**" means the common seal of the Company (if adopted) including any facsimile thereof.

"**Secretary**" means any Person appointed by the Directors to perform any of the duties of the secretary of the Company.

"**Securities Act**" means the Securities Act of 1933 of the United States of America, as amended, or any similar federal statute and the rules and regulations of the Commission thereunder, all as the same shall be in effect at the time.

"**Share**" means a share in the capital of the Company. All references to "Shares" herein shall be deemed to be Shares of any or all Classes as the context may require. For the avoidance of doubt in these Articles the expression "Share" shall include a fraction of a Share.

"**Shareholder**" or "**Member**" means a Person who is registered as the holder of Shares in the Register and includes each subscriber to the Memorandum of Association pending entry in the Register of such subscriber.

"**Share Premium Account**" means the share premium account established in accordance with these Articles and the Companies Law.

"**signed**" means bearing a signature or representation of a signature affixed by mechanical means.

"**Special Resolution**" means a special resolution of the Company passed in accordance with the Companies Law, being a resolution:

(a) passed by a majority of not less than two-thirds of such Shareholders as, being entitled to do so, vote in person or, where proxies are allowed, by proxy at a general meeting of the Company of which notice specifying the intention to propose the resolution as a special resolution has been duly given and where a poll is taken regard shall be had in computing a majority to the number of votes to which each Shareholder is entitled; or

(b) approved in writing by all of the Shareholders entitled to vote at a general meeting of the Company in one or more instruments each signed by one or more of the Shareholders and the effective date of the special resolution so adopted shall be the date on which the instrument or the last of such instruments, if more than one, is executed.

"**Treasury Shares**" means Shares that were previously issued but were purchased, redeemed, surrendered or otherwise acquired by the Company and not cancelled.

2. In these Articles, save where the context requires otherwise:

(a) words importing the singular number shall include the plural number and vice versa;

(b) words importing the masculine gender only shall include the feminine gender and any Person as the context may require;

(c) the word "may" shall be construed as permissive and the word "shall" shall be construed as imperative;

(d) reference to a dollar or dollars or USD (or $) and to a cent or cents is reference to dollars and cents of the United States of America;

(e) reference to a statutory enactment shall include reference to any amendment or re-enactment thereof for the time being in force;

(f) reference to any determination by the Directors shall be construed as a determination by the Directors in their sole and absolute discretion and shall be applicable either generally or in any particular case; and

(g) reference to "in writing" shall be construed as written or represented by any means reproducible in writing, including any form of print, lithograph, email, facsimile, photograph or telex or represented by any other substitute or format for storage or transmission for writing or partly one and partly another.

3. Subject to the preceding Articles, any words defined in the Companies Law shall, if not inconsistent with the subject or context, bear the same meaning in these Articles.

**PRELIMINARY**

4. The business of the Company may be commenced at any time after incorporation.

5. The Office shall be at such address in the Cayman Islands as the Directors may from time to time determine. The Company may in addition establish and maintain such other offices and places of business and agencies in such places as the Directors may from time to time determine.

6. The expenses incurred in the formation of the Company and in connection with the offer for subscription and issue of Shares shall be paid by the Company. Such expenses may be amortised over such period as the Directors may determine and the amount so paid shall be charged against income and/or capital in the accounts of the Company as the Directors shall determine.

7. The Directors shall keep, or cause to be kept, the Register at such place or (subject to compliance with the Companies Law and these Articles) places as the Directors may from time to time determine (provided that the Register shall, at all times, be kept outside the United Kingdom). In the absence of any such determination, the Register shall be kept at the Office. The Directors may keep, or cause to be kept, one or more Branch Registers as well as the Principal Register in accordance with the Companies Law, provided always that a duplicate of such Branch Register(s) shall be maintained with the Principal Register in accordance with the Companies Law and the rules or requirements of any Designated Stock Exchange.

**SHARES**

8. Subject to these Articles and, where applicable, the rules of the Designated Stock Exchange, all Shares for the time being unissued shall be under the control of the Directors who may:

(a) issue, allot and dispose of the same to such Persons, in such manner, on such terms and having such rights and being subject to such restrictions as they may from time to time determine; and

(b) grant options with respect to such Shares and issue warrants or similar instruments with respect thereto;

and, for such purposes, the Directors may reserve an appropriate number of Shares for the time being unissued.

9. The Directors, or the Shareholders by Ordinary Resolution, may authorise the division of Shares into any number of Classes and sub-classes and the different Classes and sub-classes shall be authorised, established and designated (or re-designated as the case may be) and the variations in the relative rights (including, without limitation, voting, dividend and redemption rights), restrictions, preferences, privileges and payment obligations as between the different Classes (if any) may be fixed and determined by the Directors or the Shareholders by Ordinary Resolution.

10. The Company may insofar as may be permitted by law, pay a commission to any Person in consideration of his subscribing or agreeing to subscribe whether absolutely or conditionally for any Shares. Such commissions may be satisfied by the payment of cash or the lodgement of fully or partly paid-up Shares or partly in one way and partly in the other. The Company may also pay such brokerage as may be lawful on any issue of Shares.

11. The Directors may refuse to accept any application for Shares, and may accept any application in whole or in part, for any reason or for no reason.

## MODIFICATION OF RIGHTS

12. Whenever the capital of the Company is divided into different Classes (and as otherwise determined by the Directors) the rights attached to any such Class may, subject to any rights or restrictions for the time being attached to any Class only be materially adversely varied or abrogated with the consent in writing of the holders of not less than two-thirds of the issued Shares of the relevant Class, or with the sanction of a resolution passed at a separate meeting of the holders of the Shares of such Class by a majority of two-thirds of the votes cast at such a meeting. To every such separate meeting all the provisions of these Articles relating to general meetings of the Company or to the proceedings thereat shall, mutatis mutandis, apply, except that the necessary quorum shall be one or more Persons at least holding or representing by proxy one-third in nominal or par value amount of the issued Shares of the relevant Class (but so that if at any adjourned meeting of such holders a quorum as above defined is not present, those Shareholders who are present shall form a quorum) and that, subject to any rights or restrictions for the time being attached to the Shares of that Class, every Shareholder of the Class shall on a poll have one vote for each Share of the Class held by him. For the purposes of this Article the Directors may treat all the Classes or any two or more Classes as forming one Class if they consider that all such Classes would be affected in the same way by the proposals under consideration, but in any other case shall treat them as separate Classes. The Directors may vary the rights attaching to any Class without the consent or approval of Shareholders provided that the rights will not, in the determination of the Directors, be materially adversely varied or abrogated by such action.

13. The rights conferred upon the holders of the Shares of any Class issued with preferred or other rights shall not, subject to any rights or restrictions for the time being attached to the Shares of that Class, be deemed to be materially adversely varied or abrogated by, *inter alia*, the creation, allotment or issue of further Shares ranking pari passu with or subsequent to them or the redemption or purchase of any Shares of any Class by the Company.

## CERTIFICATES

14. No Person shall be entitled to a certificate for any or all of his Shares, unless the Directors shall determine otherwise.

15. Every share certificate of the Company shall bear any legends required under applicable laws, including the Securities Act. If any share certificate is lost, destroyed or stolen, the Directors may require the holder or holders of the relevant Share to provide an indemnity in a form acceptable to the Directors. Upon such indemnity being provided, a new share certificate may be issued to the holder or holders entitled to such lost, destroyed or stolen share certificate, unless the Directors determine otherwise.

## FRACTIONAL SHARES

16. The Directors may issue fractions of a Share and, if so issued, a fraction of a Share shall be subject to and carry the corresponding fraction of liabilities (whether with respect to nominal or par value, premium, contributions, calls or otherwise), limitations, preferences, privileges, qualifications, restrictions, rights (including, without prejudice to the generality of the foregoing, voting and participation rights) and other attributes of a whole Share. If more than one fraction of a Share of the same Class is issued to or acquired by the same Shareholder such fractions shall be accumulated.

## LIEN

17. The Company has a first and paramount lien on every Share (whether or not fully paid) for all amounts (whether presently payable or not) payable at a fixed time or called in respect of that Share. The Company also has a first and paramount lien on every Share (whether or not fully paid) registered in the name of a Person indebted or under liability to the Company (whether he is the sole registered holder of a Share or one of two or more joint holders) for all amounts owing by him or his estate to the Company (whether or not presently payable). The Directors may at any time declare a Share to be wholly or in part exempt from the provisions of this Article. The Company’s lien on a Share extends to any amount payable in respect of it.

18. The Company may sell, in such manner as the Directors may determine, any Share on which the Company has a lien, but no sale shall be made unless an amount in respect of which the lien exists is presently payable nor until the expiration of fourteen days after a notice in writing, demanding payment of such part of the amount in respect of which the lien exists as is presently payable, has been given to the registered holder for the time being of the Share, or the Persons entitled thereto by reason of his death or bankruptcy.

19. For giving effect to any such sale the Directors may authorise some Person to transfer the Shares sold to the purchaser thereof. The purchaser shall be registered as the holder of the Shares comprised in any such transfer and he shall not be bound to see to the application of the purchase money, nor shall his title to the Shares be affected by any irregularity or invalidity in the proceedings in reference to the sale.

20. The proceeds of the sale after deduction of expenses, fees and commission incurred by the Company shall be received by the Company and applied in payment of such part of the amount in respect of which the lien exists as is presently payable, and the residue shall (subject to a like lien for sums not presently payable as existed upon the Shares prior to the sale) be paid to the Person entitled to the Shares immediately prior to the sale.

## CALLS ON SHARES

21. The Directors may from time to time make calls upon the Shareholders in respect of any moneys unpaid on their Shares, and each Shareholder shall (subject to receiving at least fourteen days' notice specifying the time or times of payment) pay to the Company at the time or times so specified the amount called on such Shares.

22. The joint holders of a Share shall be jointly and severally liable to pay calls in respect thereof.

23. If a sum called in respect of a Share is not paid before or on the day appointed for payment thereof, the Person from whom the sum is due shall pay interest upon the sum at the rate of eight percent per annum from the day appointed for the payment thereof to the time of the actual payment, but the Directors shall be at liberty to waive payment of that interest wholly or in part.

24. The provisions of these Articles as to the liability of joint holders and as to payment of interest shall apply in the case of non-payment of any sum which, by the terms of issue of a Share, becomes payable at a fixed time, whether on account of the amount of the Share, or by way of premium, as if the same had become payable by virtue of a call duly made and notified.

25. The Directors may make arrangements on the issue of partly paid Shares for a difference between the Shareholders, or the particular Shares, in the amount of calls to be paid and in the times of payment.

26. The Directors may, if they think fit, receive from any Shareholder willing to advance the same all or any part of the moneys uncalled and unpaid upon any partly paid Shares held by him, and upon all or any of the moneys so advanced may (until the same would, but for such advance, become presently payable) pay interest at such rate (not exceeding without the sanction of an Ordinary Resolution, eight percent per annum) as may be agreed upon between the Shareholder paying the sum in advance and the Directors.

## FORFEITURE OF SHARES

27. If a Shareholder fails to pay any call or instalment of a call in respect of any Shares on the day appointed for payment, the Directors may, at any time thereafter during such time as any part of such call or instalment remains unpaid, serve a notice on him requiring payment of so much of the call or instalment as is unpaid, together with any interest which may have accrued.

28. The notice shall name a further day (not earlier than the expiration of fourteen days from the date of the notice) on or before which the payment required by the notice is to be made, and shall state that in the event of non-payment at or before the time appointed the Shares in respect of which the call was made will be liable to be forfeited.

29. If the requirements of any such notice as aforesaid are not complied with, any Share in respect of which the notice has been given may at any time thereafter, before the payment required by notice has been made, be forfeited by a resolution of the Directors to that effect.

30. A forfeited Share may be sold or otherwise disposed of on such terms and in such manner as the Directors think fit, and at any time before a sale or disposition the forfeiture may be cancelled on such terms as the Directors think fit.

31. A Person whose Shares have been forfeited shall cease to be a Shareholder in respect of the forfeited Shares, but shall, notwithstanding, remain liable to pay to the Company all moneys which at the date of forfeiture were payable by him to the Company in respect of the Shares forfeited, but his liability shall cease if and when the Company receives payment in full of the amount unpaid on the Shares forfeited.

32. A statutory declaration in writing that the declarant is a Director, and that a Share has been duly forfeited on a date stated in the declaration, shall be conclusive evidence of the facts in the declaration as against all Persons claiming to be entitled to the Share.

33. The Company may receive the consideration, if any, given for a Share on any sale or disposition thereof pursuant to the provisions of these Articles as to forfeiture and may execute a transfer of the Share in favour of the Person to whom the Share is sold or disposed of and that Person shall be registered as the holder of the Share, and shall not be bound to see to the application of the purchase money, if any, nor shall his title to the Shares be affected by any irregularity or invalidity in the proceedings in reference to the disposition or sale.

34. The provisions of these Articles as to forfeiture shall apply in the case of non-payment of any sum which by the terms of issue of a Share becomes due and payable, whether on account of the amount of the Share, or by way of premium, as if the same had been payable by virtue of a call duly made and notified.

## TRANSFER OF SHARES

35. Subject to these Articles and the rules or regulations of the Designated Stock Exchange or any relevant securities laws, any Member may transfer all or any Shares by an instrument of transfer in the usual or common form or in a form prescribed by the Designated Stock Exchange or in any other form approved by the Directors and may be under hand or, if the transferor or transferee is a clearing house or its nominee(s), by hand or by machine imprinted signature or by such other manner of execution as the Directors may approve from time to time.

36. The instrument of transfer of any Share shall be executed by or on behalf of the transferor and if in respect of a nil or partly paid up Share, or if so required by the Directors, shall also be executed on behalf of the transferee and shall be accompanied by the certificate (if any) of the Shares to which it relates and such other evidence as the Directors may reasonably require to show the right of the transferor to make the transfer. The transferor shall be deemed to remain a Shareholder until the name of the transferee is entered in the Register in respect of the relevant Shares.

37. Subject to the rules of any Designated Stock Exchange on which the Shares in question may be listed and to any rights and restrictions for the time being attached to any Share, the Directors may in their absolute discretion decline to register any transfer of Shares without assigning any reason therefor. If the Directors refuse to register a transfer of any Share the Secretary shall, within two months after the date on which the transfer request was lodged with the Company, send to the transferor and transferee notice of the refusal.

38. Subject to the provisions of these Articles and rules of any Designated Stock Exchange on which the shares in question may be listed and to any rights and restrictions for the time being attached to any Share, the registration of transfers may be suspended and the Register closed at such times and for such periods as the Directors may from time to time determine.

39. All instruments of transfer that are registered shall be retained by the Company, but any instrument of transfer that the Directors decline to register shall (except in any case of fraud) be returned to the Person depositing the same.

## TRANSMISSION OF SHARES

40. The legal personal representative of a deceased sole holder of a Share shall be the only Person recognised by the Company as having any title to the Share. In the case of a Share registered in the name of two or more holders, the survivors or survivor, or the legal personal representatives of the deceased holder of the Share, shall be the only Person recognised by the Company as having any title to the Share.

41. Any Person becoming entitled to a Share in consequence of the death or bankruptcy of a Shareholder shall upon such evidence being produced as may from time to time be required by the Directors, have the right either to be registered as a Shareholder in respect of the Share or, instead of being registered himself, to make such transfer of the Share as the deceased or bankrupt Person could have made; but the Directors shall, in either case, have the same right to decline or suspend registration as they would have had in the case of a transfer of the Share by the deceased or bankrupt Person before the death or bankruptcy.

42. A Person becoming entitled to a Share by reason of the death or bankruptcy of a Shareholder shall be entitled to the same dividends and other advantages to which he would be entitled if he were the registered Shareholder, except that he shall not, before being registered as a Shareholder in respect of the Share, be entitled in respect of it to exercise any right conferred by membership in relation to meetings of the Company.

## ALTERATION OF SHARE CAPITAL

43. The Company may from time to time by Ordinary Resolution increase the share capital by such sum, to be divided into Shares of such Classes and amount, as the resolution shall prescribe.

44. The Company may by Ordinary Resolution:

(a) consolidate and divide all or any of its share capital into Shares of a larger amount than its existing Shares;

(b) convert all or any of its paid up Shares into stock and reconvert that stock into paid up Shares of any denomination;

(c) subdivide its existing Shares, or any of them into Shares of a smaller amount provided that in the subdivision the proportion between the amount paid and the amount, if any, unpaid on each reduced Share shall be the same as it was in case of the Share from which the reduced Share is derived; and

(d) cancel any Shares that, at the date of the passing of the resolution, have not been taken or agreed to be taken by any Person and diminish the amount of its share capital by the amount of the Shares so cancelled.

45. The Company may by Special Resolution reduce its share capital and any capital redemption reserve in any manner authorised by law.

## REDEMPTION, PURCHASE AND SURRENDER OF SHARES

46. Subject to the Companies Law, the Company may:

(a) issue Shares on terms that they are to be redeemed or are liable to be redeemed at the option of the Company or the Shareholder on such terms and in such manner as the Directors may determine;

(b) purchase its own Shares (including any redeemable Shares) on such terms and in such manner as the Directors may determine and agree with the Shareholder;

(c) make a payment in respect of the redemption or purchase of its own Shares in any manner authorised by the Companies Law, including out of its capital; and

(d) accept the surrender for no consideration of any paid up Share (including any redeemable Share) on such terms and in such manner as the Directors may determine.

47. Any Share in respect of which notice of redemption has been given shall not be entitled to participate in the profits of the Company in respect of the period after the date specified as the date of redemption in the notice of redemption.

48. The redemption, purchase or surrender of any Share shall not be deemed to give rise to the redemption, purchase or surrender of any other Share.

49. The Directors may when making payments in respect of redemption or purchase of Shares, if authorised by the terms of issue of the Shares being redeemed or purchased or with the agreement of the holder of such Shares, make such payment either in cash or in specie including, without limitation, interests in a special purpose vehicle holding assets of the Company or holding entitlement to the proceeds of assets held by the Company or in a liquidating structure.

## TREASURY SHARES

50. Shares that the Company purchases, redeems or acquires (by way of surrender or otherwise) may, at the option of the Company, be cancelled immediately or held as Treasury Shares in accordance with the Companies Law. In the event that the Directors do not specify that the relevant Shares are to be held as Treasury Shares, such Shares shall be cancelled.

51. No dividend may be declared or paid, and no other distribution (whether in cash or otherwise) of the Company's assets (including any distribution of assets to members on a winding up) may be declared or paid in respect of a Treasury Share.

52. The Company shall be entered in the Register as the holder of the Treasury Shares provided that:

(a) the Company shall not be treated as a member for any purpose and shall not exercise any right in respect of the Treasury Shares, and any purported exercise of such a right shall be void;

(b) a Treasury Share shall not be voted, directly or indirectly, at any meeting of the Company and shall not be counted in determining the total number of issued shares at any given time, whether for the purposes of these Articles or the Companies Law, save that an allotment of Shares as fully paid bonus shares in respect of a Treasury Share is permitted and Shares allotted as fully paid bonus shares in respect of a treasury share shall be treated as Treasury Shares.

53. Treasury Shares may be disposed of by the Company on such terms and conditions as determined by the Directors.

## GENERAL MEETINGS

54. The Directors may, whenever they think fit, convene a general meeting of the Company.

55. For so long as the Company's Shares are traded on a Designated Stock Exchange, the Company shall in each year hold a general meeting as its annual general meeting at such time and place as may be determined by the Directors.

56. The Directors may cancel or postpone any duly convened general meeting at any time prior to such meeting, except for general meetings requisitioned by the Shareholders in accordance with these Articles, for any reason or for no reason at any time prior to the time for holding such meeting or, if the meeting is adjourned, the time for holding such adjourned meeting. The Directors shall give Shareholders notice in writing of any cancellation or postponement. A postponement may be for a stated period of any length or indefinitely as the Directors may determine.

57. General meetings shall also be convened on the requisition in writing of any Shareholder or Shareholders entitled to attend and vote at general meetings of the Company and to exercise at least a majority of the votes permitted to be exercised at any such meeting deposited at the Office specifying the objects of the meeting by notice given no later than 21 days from the date of deposit of the requisition signed by the requisitionists, and if the Directors do not convene such meeting for a date not later than 45 days after the date of such deposit, the requisitionists themselves may convene the general meeting in the same manner, as nearly as possible, as that in which general meetings may be convened by the Directors, and all reasonable expenses incurred by the requisitionists as a result of the failure of the Directors to convene the general meeting shall be reimbursed to them by the Company.

58. If at any time there are no Directors, any two Shareholders (or if there is only one Shareholder then that Shareholder) entitled to vote at general meetings of the Company may convene a general meeting in the same manner as nearly as possible as that in which general meetings may be convened by the Directors.

## NOTICE OF GENERAL MEETINGS

59. At least twenty one (21) clear days' notice of a general meeting in writing counting from the date service is deemed to take place as provided in these Articles specifying the place, the day and the hour of the meeting and the general nature of the business, shall be given in the manner hereinafter provided or in such other manner (if any) as may be prescribed by the Company by Ordinary Resolution to such Persons as are, under these Articles, entitled to receive such notices from the Company, but with the consent of all the Shareholders entitled to receive notice of some particular meeting and attend and vote thereat, that meeting may be convened by such shorter notice or without notice and in such manner as those Shareholders may think fit.

60. The accidental omission to give notice of a meeting to or the non-receipt of a notice of a meeting by any Shareholder shall not invalidate the proceedings at any meeting.

## PROCEEDINGS AT GENERAL MEETINGS

61. All business carried out at a general meeting shall be deemed special with the exception of sanctioning a dividend, the consideration of the accounts, balance sheets, any report of the Directors or of the Company's auditors, and the fixing of the remuneration of the Company's auditors. No special business shall be transacted at any general meeting without the consent of all Shareholders entitled to receive notice of that meeting unless notice of such special business has been given in the notice convening that meeting. In addition, no business may be transacted at any general meeting, other than business that is either specified in the notice of the meeting given by or at the direction of the Directors (or any duly authorised committee thereof) (including on the requisition of Shareholders in accordance with these Articles) or otherwise properly brought before an annual general meeting by or at the direction of the Directors (or any duly authorised committee thereof).

62. No business shall be transacted at any general meeting unless a quorum of Shareholders is present at the time when the meeting proceeds to business. Save as otherwise provided by these Articles, one or more Shareholders holding at least one third of the paid up voting share capital of the Company present in person or by proxy and entitled to vote at that meeting shall form a quorum.

63. If within half an hour from the time appointed for the meeting a quorum is not present, the meeting, if convened upon the requisition of Shareholders, shall be dissolved. In any other case it shall stand adjourned to the same day in the next week, at the same time and place, and if at the adjourned meeting a quorum is not present within half an hour from the time appointed for the meeting the Shareholder or Shareholders present and entitled to vote shall form a quorum.

64. If the Directors wish to make this facility available for a specific general meeting or all general meetings of the Company, participation in any general meeting of the Company may be by means of a telephone or similar communication equipment by way of which all Persons participating in such meeting can communicate with each other and such participation shall be deemed to constitute presence in person at the meeting.

65. The chairman, if any, of the board of Directors shall preside as chairman at every general meeting of the Company.

66. If there is no such chairman, or if at any general meeting he is not present within fifteen minutes after the time appointed for holding the meeting or is unwilling to act as chairman, any Director or Person nominated by the Directors shall preside as chairman, failing which the Shareholders present in person or by proxy shall choose any Person present to be chairman of that meeting.

67. The chairman may adjourn a meeting from time to time and from place to place either:

(a) with the consent of any general meeting at which a quorum is present (and shall if so directed by the meeting); or

(b) without the consent of such meeting if, in his sole opinion, he considers it necessary to do so to:

(i) secure the orderly conduct or proceedings of the meeting; or

(ii) give all persons present in person or by proxy and having the right to speak and / or vote at such meeting, the ability to do so,

but no business shall be transacted at any adjourned meeting other than the business left unfinished at the meeting from which the adjournment took place. When a meeting, or adjourned meeting, is adjourned for fourteen days or more, notice of the adjourned meeting shall be given in the manner provided for the original meeting. Save as aforesaid, it shall not be necessary to give any notice of an adjournment or of the business to be transacted at an adjourned meeting.

68. At any general meeting a resolution put to the vote of the meeting shall be decided on a show of hands, unless a poll is (before or on the declaration of the result of the show of hands) demanded by the chairman or one or more Shareholders present in person or by proxy entitled to vote, and unless a poll is so demanded, a declaration by the chairman that a resolution has, on a show of hands, been carried, or carried unanimously, or by a particular majority, or lost, and an entry to that effect in the book of the proceedings of the Company, shall be conclusive evidence of the fact, without proof of the number or proportion of the votes recorded in favour of, or against, that resolution.

69. At any annual general meeting where a resolution for the election of directors is proposed in accordance with these Articles, a plurality of the votes cast shall be sufficient to elect a Director.

70. If a poll is duly demanded it shall be taken in such manner as the chairman directs, and the result of the poll shall be deemed to be the resolution of the meeting at which the poll was demanded.

71. In the case of an equality of votes, whether on a show of hands or on a poll, the chairman of the meeting at which the show of hands takes place or at which the poll is demanded, shall not be entitled to a second or casting vote.

72. A poll demanded on the election of a chairman of the meeting or on a question of adjournment shall be taken forthwith. A poll demanded on any other question shall be taken at such time as the chairman of the meeting directs.

## VOTES OF SHAREHOLDERS

73. Subject to any rights and restrictions for the time being attached to any Share, on a show of hands every Shareholder present in person and every Person representing a Shareholder by proxy shall, at a general meeting of the Company, each have one vote and on a poll every Shareholder and every Person representing a Shareholder by proxy shall have one vote for each Share of which he or the Person represented by proxy is the holder.

74. In the case of joint holders the vote of the senior who tenders a vote whether in person or by proxy shall be accepted to the exclusion of the votes of the other joint holders and for this purpose seniority shall be determined by the order in which the names stand in the Register.

75. A Shareholder of unsound mind, or in respect of whom an order has been made by any court having jurisdiction in lunacy, may vote in respect of Shares carrying the right to vote held by him, whether on a show of hands or on a poll, by his committee, or other Person in the nature of a committee appointed by that court, and any such committee or other Person, may vote in respect of such Shares by proxy.

76. No Shareholder shall be entitled to vote at any general meeting of the Company unless all calls, if any, or other sums presently payable by him in respect of Shares carrying the right to vote held by him have been paid.

77. On a poll votes may be given either personally or by proxy.

78. The instrument appointing a proxy shall be in writing under the hand of the appointor or of his attorney duly authorised in writing or, if the appointor is a corporation, either under Seal or under the hand of an Officer or attorney duly authorised. A proxy need not be a Shareholder.

79. An instrument appointing a proxy may be in any usual or common form or such other form as the Directors may approve.

80. The instrument appointing a proxy shall be deposited at the Office or at such other place as is specified for that purpose in the notice convening the meeting no later than the time for holding the meeting or, if the meeting is adjourned, the time for holding such adjourned meeting.

81. The instrument appointing a proxy shall be deemed to confer authority to demand or join in demanding a poll.

82. A resolution in writing signed by all the Shareholders for the time being entitled to receive notice of and to attend and vote at general meetings of the Company (or being corporations by their duly authorised representatives) shall be as valid and effective as if the same had been passed at a general meeting of the Company duly convened and held.

## CORPORATIONS ACTING BY REPRESENTATIVES AT MEETINGS

83. Any corporation which is a Shareholder or a Director may by resolution of its directors or other governing body authorise such Person as it thinks fit to act as its representative at any meeting of the Company or of any meeting of holders of a Class or of the Directors or of a committee of Directors, and the Person so authorised shall be entitled to exercise the same powers on behalf of the corporation which he represents as that corporation could exercise if it were an individual Shareholder or Director.

## CLEARING HOUSES

84. If a clearing house (or its nominee) is a Member of the Company it may, by resolution of its directors or other governing body or by power of attorney, authorise such person or persons as it thinks fit to act as its representative or representatives at any general meeting of the Company or at any general meeting of any class of Members of the Company provided that, if more than one person is so authorised, the authorisation shall specify the number and class of Shares in respect of which each such person is so authorised. A person so authorised pursuant to this Article shall be entitled to exercise the same powers on behalf of the clearing house (or its nominee) which he represents as that clearing house (or its nominee) could exercise if it were an individual Member holding the number and Class of Shares specified in such authorisation.

## DIRECTORS

85. The name(s) of the first Director(s) shall either be determined in writing by a majority (or in the case of a sole subscriber that subscriber) of, or elected at a meeting of, the subscribers of the Memorandum of Association.

86. The Directors shall be divided into three (3) classes designated as Class I, Class II and Class III, respectively. Directors shall be assigned to each class in accordance with a resolution or resolutions adopted by the board of Directors. At the first annual general meeting of Members, the term of office of the Class I Directors shall expire and Class I Directors appointed at such meeting shall be elected for a full term of three (3) years. At the second annual general meeting of Members, the term of office of the Class II Directors shall expire and Class II Directors appointed at such meeting shall be elected for a full term of three (3) years. At the third annual general meeting of Members, the term of office of the Class III Directors shall expire and Class III Directors at such meeting appointed shall be elected for a full term of three (3) years. At each succeeding annual general meeting of Members, Directors shall be elected for a full term of three (3) years to succeed the Directors of the class whose terms expire at such annual general meeting. Notwithstanding the foregoing provisions of this Article, each Director shall hold office until the expiration of his term, until his successor shall have been duly elected and qualified or until his earlier death, resignation or removal. No decrease in the number of Directors constituting the board of Directors shall shorten the term of any incumbent Director.

87. The board of Directors shall in each case prior to an annual general meeting determine the maximum number of Directors to be appointed at each annual general meeting. At any annual general meeting where a resolution for the election of directors is proposed in accordance with these Articles, a plurality of the votes cast shall be sufficient to elect a Director.

88. Subject to these Articles, a Director shall hold office until such time as he is removed from office by Ordinary Resolution.

89. The board of Directors may from time to time fix the maximum and minimum number of Directors to be appointed but unless such numbers are fixed as aforesaid the minimum number of Directors shall be one and the maximum number of Directors shall be unlimited.

90. The remuneration of the Directors may be determined by the Directors.

91. There shall be no shareholding qualification for Directors.

92. The Directors shall have power at any time and from time to time to appoint any Person to be a Director, either as a result of a casual vacancy or as an additional Director, subject to the maximum number (if any) imposed and assign such Director to such class as they may determine.

## ALTERNATE DIRECTOR

93. Any Director may in writing appoint another Person to be his alternate and, save to the extent provided otherwise in the form of appointment, such alternate shall have authority to sign written resolutions on behalf of the appointing Director, but shall not be authorised to sign such written resolutions where they have been signed by the appointing Director, and to act in such Director's place at any meeting of the Directors. Every such alternate shall be entitled to attend and vote at meetings of the Directors as the alternate of the Director appointing him and where he is a Director to have a separate vote in addition to his own vote. A Director may at any time in writing revoke the appointment of an alternate appointed by him. Such alternate shall not be an Officer solely as a result of his appointment as an alternate other than in respect of such times as the alternate acts as a Director. The remuneration of such alternate shall be payable out of the remuneration of the Director appointing him and the proportion thereof shall be agreed between them.

## POWERS AND DUTIES OF DIRECTORS

94. Subject to the Companies Law, these Articles and to any resolutions passed in a general meeting, the business of the Company shall be managed by the Directors, who may pay all expenses incurred in setting up and registering the Company and may exercise all powers of the Company. No resolution passed by the Company in general meeting shall invalidate any prior act of the Directors that would have been valid if that resolution had not been passed.

95. The Directors may from time to time appoint any Person, whether or not a Director to hold such office in the Company as the Directors may think necessary for the administration of the Company, including but not limited to, the office of president, one or more vice-presidents, treasurer, assistant treasurer, manager or controller, and for such term and at such remuneration (whether by way of salary or commission or participation in profits or partly in one way and partly in another), and with such powers and duties as the Directors may think fit. Any Person so appointed by the Directors may be removed by the Directors or by the Company by Ordinary Resolution. The Directors may also appoint one or more of their number to the office of managing director upon like terms, but any such appointment shall ipso facto terminate if any managing director ceases from any cause to be a Director, or if the Company by Ordinary Resolution resolves that his tenure of office be terminated.

96. The Directors may appoint any Person to be a Secretary (and if need be an assistant Secretary or assistant Secretaries) who shall hold office for such term, at such remuneration and upon such conditions and with such powers as they think fit. Any Secretary or assistant Secretary so appointed by the Directors may be removed by the Directors or by the Company by Ordinary Resolution.

97. The Directors may delegate any of their powers to committees consisting of such member or members of their body as they think fit; any committee so formed shall in the exercise of the powers so delegated conform to any regulations that may be imposed on it by the Directors.

98. The Directors may from time to time and at any time by power of attorney (whether under Seal or under hand) or otherwise appoint any company, firm or Person or body of Persons, whether nominated directly or indirectly by the Directors, to be the attorney or attorneys or authorised signatory (any such person being an "**Attorney**" or "**Authorised Signatory**", respectively) of the Company for such purposes and with such powers, authorities and discretion (not exceeding those vested in or exercisable by the Directors under these Articles) and for such period and subject to such conditions as they may think fit, and any such power of attorney or other appointment may contain such provisions for the protection and convenience of Persons dealing with any such Attorney or Authorised Signatory as the Directors may think fit, and may also authorise any such Attorney or Authorised Signatory to delegate all or any of the powers, authorities and discretion vested in him.

99. The Directors may from time to time provide for the management of the affairs of the Company in such manner as they shall think fit and the provisions contained in the three next following Articles shall not limit the general powers conferred by this Article.

100. The Directors from time to time and at any time may establish any committees, local boards or agencies for managing any of the affairs of the Company and may appoint any Person to be a member of such committees or local boards and may appoint any managers or agents of the Company and may fix the remuneration of any such Person.

101. The Directors from time to time and at any time may delegate to any such committee, local board, manager or agent any of the powers, authorities and discretions for the time being vested in the Directors and may authorise the members for the time being of any such local board, or any of them to fill any vacancies therein and to act notwithstanding vacancies and any such appointment or delegation may be made on such terms and subject to such conditions as the Directors may think fit and the Directors may at any time remove any Person so appointed and may annul or vary any such delegation, but no Person dealing in good faith and without notice of any such annulment or variation shall be affected thereby.

102. Any such delegates as aforesaid may be authorised by the Directors to sub-delegate all or any of the powers, authorities, and discretion for the time being vested in them.

103. The Directors may agree with a Shareholder to waive or modify the terms applicable to such Shareholder's subscription for Shares without obtaining the consent of any other Shareholder; provided that such waiver or modification does not amount to a variation or abrogation of the rights attaching to the Shares of such other Shareholders.

## BORROWING POWERS OF DIRECTORS

104. The Directors may exercise all the powers of the Company to borrow money and to mortgage or charge its undertaking, property and uncalled capital or any part thereof, or to otherwise provide for a security interest to be taken in such undertaking, property or uncalled capital, and to issue debentures, debenture stock and other securities whenever money is borrowed or as security for any debt, liability or obligation of the Company or of any third party.

## THE SEAL

105. The Seal shall not be affixed to any instrument except by the authority of a resolution of the Directors provided always that such authority may be given prior to or after the affixing of the Seal and if given after may be in general form confirming a number of affixings of the Seal. The Seal shall be affixed in the presence of a Director or a Secretary (or an assistant Secretary) or in the presence of any one or more Persons as the Directors may appoint for the purpose and every Person as aforesaid shall sign every instrument to which the Seal is so affixed in their presence.

106. The Company may maintain a facsimile of the Seal in such countries or places as the Directors may appoint and such facsimile Seal shall not be affixed to any instrument except by the authority of a resolution of the Directors provided always that such authority may be given prior to or after the affixing of such facsimile Seal and if given after may be in general form confirming a number of affixings of such facsimile Seal. The facsimile Seal shall be affixed in the presence of such Person or Persons as the Directors shall for this purpose appoint and such Person or Persons as aforesaid shall sign every instrument to which the facsimile Seal is so affixed in their presence and such affixing of the facsimile Seal and signing as aforesaid shall have the same meaning and effect as if the Seal had been affixed in the presence of and the instrument signed by a Director or a Secretary (or an assistant Secretary) or in the presence of any one or more Persons as the Directors may appoint for the purpose.

107. Notwithstanding the foregoing, a Secretary or any assistant Secretary shall have the authority to affix the Seal, or the facsimile Seal, to any instrument for the purposes of attesting authenticity of the matter contained therein but which does not create any obligation binding on the Company.

## DISQUALIFICATION OF DIRECTORS

108. The office of Director shall be vacated, if the Director:

(a) becomes bankrupt or makes any arrangement or composition with his creditors;

(b) dies or is found to be or becomes of unsound mind;

(c) resigns his office by notice in writing to the Company;

(d) is removed from office by Ordinary Resolution; or

(e) is removed from office pursuant to any other provision of these Articles.

## PROCEEDINGS OF DIRECTORS

109. The Directors may meet together (either within or outside the Cayman Islands) for the despatch of business, adjourn, and otherwise regulate their meetings and proceedings as they think fit. Questions arising at any meeting shall be decided by a majority of votes. In case of an equality of votes the chairman shall not have a second or casting vote. A Director may, and a Secretary or assistant Secretary on the requisition of a Director shall, at any time summon a meeting of the Directors.

110. A Director may participate in any meeting of the Directors, or of any committee appointed by the Directors of which such Director is a member, by means of telephone or similar communication equipment by way of which all Persons participating in such meeting can communicate with each other and such participation shall be deemed to constitute presence in person at the meeting.

111. The quorum necessary for the transaction of the business of the Directors shall be a majority of the Directors then appointed. A Director represented by an alternate Director at any meeting shall be deemed to be present for the purposes of determining whether or not a quorum is present.

112. A Director who is in any way, whether directly or indirectly, interested in a contract or proposed contract with the Company shall declare the nature of his interest at a meeting of the Directors. A general notice given to the Directors by any Director to the effect that he is to be regarded as interested in any contract or other arrangement which may thereafter be made with that company or firm shall be deemed a sufficient declaration of interest in regard to any contract so made. A Director may vote in respect of any contract or proposed contract or arrangement notwithstanding that he may be interested therein and if he does so his vote shall be counted and he may be counted in the quorum at any meeting of the Directors at which any such contract or proposed contract or arrangement shall come before the meeting for consideration.

113. A Director may hold any other office or place of profit under the Company (other than the office of auditor) in conjunction with his office of Director for such period and on such terms (as to remuneration and otherwise) as the Directors may determine and no Director or intending Director shall be disqualified by his office from contracting with the Company either with regard to his tenure of any such other office or place of profit or as vendor, purchaser or otherwise, nor shall any such contract or arrangement entered into by or on behalf of the Company in which any Director is in any way interested, be liable to be avoided, nor shall any Director so contracting or being so interested be liable to account to the Company for any profit realised by any such contract or arrangement by reason of such Director holding that office or of the fiduciary relation thereby established. A Director, notwithstanding his interest, may be counted in the quorum present at any meeting of the Directors whereat he or any other Director is appointed to hold any such office or place of profit under the Company or whereat the terms of any such appointment are arranged and he may vote on any such appointment or arrangement.

114. Any Director may act by himself or his firm in a professional capacity for the Company, and he or his firm shall be entitled to remuneration for professional services as if he were not a Director; provided that nothing herein contained shall authorise a Director or his firm to act as auditor to the Company.

115. The Directors shall cause minutes to be made in books or loose-leaf folders provided for the purpose of recording:

(a) all appointments of Officers made by the Directors;

(b) the names of the Directors present at each meeting of the Directors and of any committee of the Directors; and

(c) all resolutions and proceedings at all meetings of the Company, and of the Directors and of committees of Directors.

116. When the chairman of a meeting of the Directors signs the minutes of such meeting the same shall be deemed to have been duly held notwithstanding that all the Directors have not actually come together or that there may have been a technical defect in the proceedings.

117. A resolution in writing signed by all the Directors or all the members of a committee of Directors entitled to receive notice of a meeting of Directors or committee of Directors, as the case may be (an alternate Director, subject as provided otherwise in the terms of appointment of the alternate Director, being entitled to sign such a resolution on behalf of his appointer), shall be as valid and effectual as if it had been passed at a duly called and constituted meeting of Directors or committee of Directors, as the case may be. When signed a resolution may consist of several documents each signed by one or more of the Directors or his duly appointed alternate.

118. The continuing Directors may act notwithstanding any vacancy in their body but if and for so long as their number is reduced below the number fixed by or pursuant to these Articles as the necessary quorum of Directors, the continuing Directors may act for the purpose of increasing the number, or of summoning a general meeting of the Company, but for no other purpose.

119. The Directors may elect a chairman of their meetings and determine the period for which he is to hold office but if no such chairman is elected, or if at any meeting the chairman is not present within fifteen minutes after the time appointed for holding the meeting, the Directors present may choose one of their number to be chairman of the meeting.

120. Subject to any regulations imposed on it by the Directors, a committee appointed by the Directors may elect a chairman of its meetings. If no such chairman is elected, or if at any meeting the chairman is not present within fifteen minutes after the time appointed for holding the meeting, the committee members present may choose one of their number to be chairman of the meeting.

121. A committee appointed by the Directors may meet and adjourn as it thinks proper. Subject to any regulations imposed on it by the Directors, questions arising at any meeting shall be determined by a majority of votes of the committee members present and in case of an equality of votes the chairman shall not have a second or casting vote.

122. All acts done by any meeting of the Directors or of a committee of Directors, or by any Person acting as a Director, shall notwithstanding that it be afterwards discovered that there was some defect in the appointment of any such Director or Person acting as aforesaid, or that they or any of them were disqualified, be as valid as if every such Person had been duly appointed and was qualified to be a Director.

## DIVIDENDS

123. Subject to any rights and restrictions for the time being attached to any Shares, or as otherwise provided for in the Companies Law and these Articles, the Directors may from time to time declare dividends (including interim dividends) and other distributions on Shares in issue and authorise payment of the same out of the funds of the Company lawfully available therefor.

124. Subject to any rights and restrictions for the time being attached to any Shares, the Company by Ordinary Resolution may declare dividends, but no dividend shall exceed the amount recommended by the Directors.

125. The Directors may determine, before recommending or declaring any dividend, to set aside out of the funds legally available for distribution such sums as they think proper as a reserve or reserves which shall be applicable for meeting contingencies, or for equalising dividends or for any other purpose to which those funds may be properly applied and pending such application may, at the determination of the Directors, either be employed in the business of the Company or be invested in such investments as the Directors may from time to time think fit.

126. Any dividend may be paid in any manner as the Directors may determine. If paid by cheque it will be sent through the post to the registered address of the Shareholder or Person entitled thereto, or in the case of joint holders, to any one of such joint holders at his registered address or to such Person and such address as the Shareholder or Person entitled, or such joint holders as the case may be, may direct. Every such cheque shall be made payable to the order of the Person to whom it is sent or to the order of such other Person as the Shareholder or Person entitled, or such joint holders as the case may be, may direct.

127. The Directors when paying dividends to the Shareholders in accordance with the foregoing provisions of these Articles may make such payment either in cash or in specie and may determine the extent to which amounts may be withheld therefrom (including, without limitation, any taxes, fees, expenses or other liabilities for which a Shareholder (or the Company, as a result of any action or inaction of the Shareholder) is liable).

128. Subject to any rights and restrictions for the time being attached to any Shares, all dividends shall be declared and paid according to the amounts paid up on the Shares, but if and for so long as nothing is paid up on any of the Shares dividends may be declared and paid according to the par value of the Shares.

129. If several Persons are registered as joint holders of any Share, any of them may give effectual receipts for any dividend or other moneys payable on or in respect of the Share.

130. No dividend shall bear interest against the Company.

## ACCOUNTS, AUDIT AND ANNUAL RETURN AND DECLARATION

131. The books of account relating to the Company's affairs shall be kept in such manner as may be determined from time to time by the Directors.

132. The books of account shall be kept at the Office, or at such other place or places as the Directors think fit, and shall always be open to the inspection of the Directors.

133. The Directors may from time to time determine whether and to what extent and at what times and places and under what conditions or regulations the accounts and books of the Company or any of them shall be open to the inspection of Shareholders not being Directors, and no Shareholder (not being a Director) shall have any right of inspecting any account or book or document of the Company except as conferred by law or authorised by the Directors or by Ordinary Resolution.

134. The accounts relating to the Company's affairs shall only be audited if the Directors so determine, in which case the financial year end and the accounting principles will be determined by the Directors.

135. The Directors in each year shall prepare, or cause to be prepared, an annual return and declaration setting forth the particulars required by the Companies Law and deliver a copy thereof to the Registrar of Companies in the Cayman Islands.

## CAPITALISATION OF RESERVES

136. Subject to the Companies Law and these Articles, the Directors may:

(a) resolve to capitalise an amount standing to the credit of reserves (including a Share Premium Account, capital redemption reserve and profit and loss account), whether or not available for distribution;

(b) appropriate the sum resolved to be capitalised to the Shareholders in proportion to the nominal amount of Shares (whether or not fully paid) held by them respectively and apply that sum on their behalf in or towards:

(i) paying up the amounts (if any) for the time being unpaid on Shares held by them respectively, or

(ii) paying up in full unissued Shares or debentures of a nominal amount equal to that sum,

and allot the Shares or debentures, credited as fully paid, to the Shareholders (or as they may direct) in those proportions, or partly in one way and partly in the other, but the Share Premium Account, the capital redemption reserve and profits which are not available for distribution may, for the purposes of this Article, only be applied in paying up unissued Shares to be allotted to Shareholders credited as fully paid;

(c) make any arrangements they think fit to resolve a difficulty arising in the distribution of a capitalised reserve and in particular, without limitation, where Shares or debentures become distributable in fractions the Directors may deal with the fractions as they think fit;

(d) authorise a Person to enter (on behalf of all the Shareholders concerned) into an agreement with the Company providing for either:

(i) the allotment to the Shareholders respectively, credited as fully paid, of Shares or debentures to which they may be entitled on the capitalisation, or

(ii) the payment by the Company on behalf of the Shareholders (by the application of their respective proportions of the reserves resolved to be capitalised) of the amounts or part of the amounts remaining unpaid on their existing Shares,

and any such agreement made under this authority being effective and binding on all those Shareholders; and

(e) generally do all acts and things required to give effect to any of the actions contemplated by this Article.

## SHARE PREMIUM ACCOUNT

137. The Directors shall in accordance with the Companies Law establish a Share Premium Account and shall carry to the credit of such account from time to time a sum equal to the amount or value of the premium paid on the issue of any Share.

138. There shall be debited to any Share Premium Account on the redemption or purchase of a Share the difference between the nominal value of such Share and the redemption or purchase price provided always that at the determination of the Directors such sum may be paid out of the profits of the Company or, if permitted by the Companies Law, out of capital.

## NOTICES

139. Any notice or document may be served by the Company or by the Person entitled to give notice to any Shareholder either personally, or by posting it airmail or air courier service in a prepaid letter addressed to such Shareholder at his address as appearing in the Register, or by electronic mail to any electronic mail address such Shareholder may have specified in writing for the purpose of such service of notices, or by facsimile should the Directors deem it appropriate. In the case of joint holders of a Share, all notices shall be given to that one of the joint holders whose name stands first in the Register in respect of the joint holding, and notice so given shall be sufficient notice to all the joint holders.

140. Any Shareholder present, either personally or by proxy, at any meeting of the Company shall for all purposes be deemed to have received due notice of such meeting and, where requisite, of the purposes for which such meeting was convened.

141. Any notice or other document, if served by:

(a) post, shall be deemed to have been served five clear days after the time when the letter containing the same is posted;

(b) facsimile, shall be deemed to have been served upon production by the transmitting facsimile machine of a report confirming transmission of the facsimile in full to the facsimile number of the recipient;

(c) recognised courier service, shall be deemed to have been served 48 hours after the time when the letter containing the same is delivered to the courier service; or

(d) electronic mail, shall be deemed to have been served immediately upon the time of the transmission by electronic mail.

In proving service by post or courier service it shall be sufficient to prove that the letter containing the notice or documents was properly addressed and duly posted or delivered to the courier service.

142. Any notice or document delivered or sent in accordance with the terms of these Articles shall notwithstanding that such Shareholder be then dead or bankrupt, and whether or not the Company has notice of his death or bankruptcy, be deemed to have been duly served in respect of any Share registered in the name of such Shareholder as sole or joint holder, unless his name shall at the time of the service of the notice or document, have been removed from the Register as the holder of the Share, and such service shall for all purposes be deemed a sufficient service of such notice or document on all Persons interested (whether jointly with or as claiming through or under him) in the Share.

143. Notice of every general meeting of the Company shall be given to:

(a) all Shareholders holding Shares with the right to receive notice and who have supplied to the Company an address for the giving of notices to them; and

(b) every Person entitled to a Share in consequence of the death or bankruptcy of a Shareholder, who but for his death or bankruptcy would be entitled to receive notice of the meeting.

No other Person shall be entitled to receive notices of general meetings.

## INDEMNITY

144. Every Director (including for the purposes of this Article any alternate Director appointed pursuant to the provisions of these Articles), Secretary, assistant Secretary, or other Officer (but not including the Company's auditors) and the personal representatives of the same (each an "**Indemnified Person**") shall be indemnified and secured harmless out of the assets and funds of the Company against all actions, proceedings, costs, charges, expenses, losses, damages or liabilities incurred or sustained by such Indemnified Person, other than by reason of such Indemnified Person's own dishonesty, wilful default or fraud as determined by a court of competent jurisdiction, in or about the conduct of the Company's business or affairs (including as a result of any mistake of judgment) or in the execution or discharge of his duties, powers, authorities or discretions, including without prejudice to the generality of the foregoing, any costs, expenses, losses or liabilities incurred by such Indemnified Person in defending (whether successfully or otherwise) any civil proceedings concerning the Company or its affairs in any court whether in the Cayman Islands or elsewhere.

145. No Indemnified Person shall be liable:

(a) for the acts, receipts, neglects, defaults or omissions of any other Director or Officer or agent of the Company; or

(b) for any loss on account of defect of title to any property of the Company; or

(c) on account of the insufficiency of any security in or upon which any money of the Company shall be invested; or

(d) for any loss incurred through any bank, broker or other similar Person; or

(e) for any loss occasioned by any negligence, default, breach of duty, breach of trust, error of judgement or oversight on such Indemnified Person's part; or

(f) for any loss, damage or misfortune whatsoever which may happen in or arise from the execution or discharge of the duties, powers, authorities, or discretions of such Indemnified Person's office or in relation thereto;

unless the same shall happen through such Indemnified Person's own dishonesty, wilful default or fraud as determined by a court of competent jurisdiction.

## NON-RECOGNITION OF TRUSTS

146. Subject to the proviso hereto, no Person shall be recognised by the Company as holding any Share upon any trust and the Company shall not, unless required by law, be bound by or be compelled in any way to recognise (even when having notice thereof) any equitable, contingent, future or partial interest in any Share or (except only as otherwise provided by these Articles or as the Companies Law requires) any other right in respect of any Share except an absolute right to the entirety thereof in each Shareholder registered in the Register, provided that, notwithstanding the foregoing, the Company shall be entitled to recognise any such interests as shall be determined by the Directors.

## WINDING UP

147. If the Company shall be wound up the liquidator shall apply the assets of the Company in such manner and order as he thinks fit in satisfaction of creditors' claims.

148. If the Company shall be wound up, the liquidator may, with the sanction of an Ordinary Resolution divide amongst the Shareholders in specie or kind the whole or any part of the assets of the Company (whether they shall consist of property of the same kind or not) and may, for such purpose set such value as he deems fair upon any property to be divided as aforesaid and may determine how such division shall be carried out as between the Shareholders or different Classes. The liquidator may, with the like sanction, vest the whole or any part of such assets in trustees upon such trusts for the benefit of the Shareholders as the liquidator, with the like sanction shall think fit, but so that no Shareholder shall be compelled to accept any assets whereon there is any liability.

## AMENDMENT OF ARTICLES OF ASSOCIATION

149. Subject to the Companies Law and the rights attaching to the various Classes, the Company may at any time and from time to time by Special Resolution alter or amend these Articles in whole or in part.

## CLOSING OF REGISTER OR FIXING RECORD DATE

150. For the purpose of determining those Shareholders that are entitled to receive notice of, attend or vote at any meeting of Shareholders or any adjournment thereof, or those Shareholders that are entitled to receive payment of any dividend, or in order to make a determination as to who is a Shareholder for any other purpose, the Directors may provide that the Register shall be closed for transfers for a stated period which shall not exceed in any case 40 days. If the Register shall be so closed for the purpose of determining those Shareholders that are entitled to receive notice of, attend or vote at a meeting of Shareholders the Register shall be so closed for at least ten days immediately preceding such meeting and the record date for such determination shall be the date of the closure of the Register.

151. In lieu of or apart from closing the Register, the Directors may fix in advance a date as the record date for any such determination of those Shareholders that are entitled to receive notice of, attend or vote at a meeting of the Shareholders and for the purpose of determining those Shareholders that are entitled to receive payment of any dividend the Directors may, at or within 90 days prior to the date of declaration of such dividend, fix a subsequent date as the record date for such determination.

152. If the Register is not so closed and no record date is fixed for the determination of those Shareholders entitled to receive notice of, attend or vote at a meeting of Shareholders or those Shareholders that are entitled to receive payment of a dividend, the date on which notice of the meeting is posted or the date on which the resolution of the Directors declaring such dividend is adopted, as the case may be, shall be the record date for such determination of Shareholders. When a determination of those Shareholders that are entitled to receive notice of, attend or vote at a meeting of Shareholders has been made as provided in this Article, such determination shall apply to any adjournment thereof.

## REGISTRATION BY WAY OF CONTINUATION

153. The Company may by Special Resolution resolve to be registered by way of continuation in a jurisdiction outside the Cayman Islands or such other jurisdiction in which it is for the time being incorporated, registered or existing. In furtherance of a resolution adopted pursuant to this Article, the Directors may cause an application to be made to the Registrar of Companies to deregister the Company in the Cayman Islands or such other jurisdiction in which it is for the time being incorporated, registered or existing and may cause all such further steps as they consider appropriate to be taken to effect the transfer by way of continuation of the Company.

## MERGERS AND CONSOLIDATION

154. The Company may merge or consolidate in accordance with the Companies Law.

155. To the extent required by the Companies Law, the Company may by Special Resolution resolve to merge or consolidate the Company.

## DISCLOSURE

156. The Directors, or any authorised service providers (including the Officers, the Secretary and the registered office agent of the Company), shall be entitled to disclose to any regulatory or judicial authority, or to any stock exchange on which the Shares may from time to time be listed, any information regarding the affairs of the Company including, without limitation, information contained in the Register and books of the Company.

**Exhibit 4.2**

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SHAREHOLDER AGREEMENT

OF

MEIRAGTX HOLDINGS PLC

DATED AS OF

_______ 2018

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**THIS SHAREHOLDER AGREEMENT** is made on April , 2018

**BETWEEN**

**(1) MEIRAGTX HOLDINGS PLC,** an exempted company incorporated in the Cayman Islands which has its registered office at Walkers Corporate Limited, Cayman Corporate Centre, 27 Hospital Road, George Town, Grand Cayman KY1-9008, Cayman Islands (the "***Company***"); and

**(2) The Persons** who are shareholders of the Company as at the date of this Agreement and any other persons who become shareholders of the Company from time to time.

**BACKGROUND**

A The Company is an exempted company limited by shares and was incorporated on May, 1 2018.

B The parties to this Agreement, other than the Company, as at the date of this Agreement, hold in aggregate 36,389,759 A Shares and 44,714,965 C Shares.

C The Company may issue additional Shares to Persons it invites to subscribe for additional shares, subject to the term of this Agreement, the Articles (as defined below) and to all applicable laws, provided such subscribers entering into a subscription agreement in a form approved by the Company from time to time.

D Members may, subject to the terms of this Agreement and to all applicable laws, transfer Shares in accordance with the Articles, provided always that no transferee shall be registered as a Member unless they have executed and delivered a Joinder Agreement (defined below) to the Company.

E Subscribers for Shares and permitted transferees (as provided by the Articles) shall be party to this Agreement on execution and delivery of the relevant Joinder Agreement.

**IT IS AGREED** as follows:

**SECTION 1. Definitions**.

As used in this Agreement, the following terms shall have the following meanings:

"***Act***" means the Companies Law (as amended) of the Cayman Islands, as amended from time to time.

“ ***Affiliate***” shall mean, as to any Person, (i) any Affiliated Fund of such Person; (ii) any other Person that, directly or indirectly, controls or is controlled by that Person, or is under common control with that Person; and (iii) in the case of a Person which is an individual, any spouse, co-habitee and/or lineal descendants by blood or adoption or any person or persons acting in its or their capacity as trustee or trustees of a trust of which such individual is the settlor. For the purposes of this definition, “***control***” shall mean the power, directly or indirectly, either to (i) vote 50% or more of the securities having ordinary voting power for the election of directors (or persons performing similar functions) of a Person or (ii) direct or cause the direction of the management and policies of a Person, whether through the ability to exercise voting power, by ownership of voting securities, contract or otherwise. The terms “***controlled by***” and “***under common control with***” have the meanings correlative thereto.

“***Affiliated Fund***” shall mean any Person (other than a natural Person) that is (or will be) engaged in making, purchasing, holding or otherwise investing in commercial loans, debt or equity investments and that is administered or managed or advised by (i) a Member, (ii) an Affiliate of a Member or (iii) an entity or an Affiliate of an entity that administers or manages or advises a Member.

“***Articles***” means the articles of association of the Company from time to time.

“***A Shares***” the A ordinary shares of US$0.00001 each in the capital of the Company.

“***Board of Directors***” means the Board of Directors designated pursuant to Section 4.1 hereof.

“***Company***” has the meaning set forth in the first paragraph of this Agreement.

“***Confidential Information***” has the meaning set forth in Section 3.6.

“***C Shareholder Majority***” means the holders of C Shares holding a majority of the total voting rights of holders of C Shares.

“ ***C Shares***” means the convertible preferred C Shares of US$0.00001 each in the capital of the Company.

“***Director*** “ means the directors of the Company from time to time, appointed in accordance with Section 4.1.

“***Effective Date*”** means                    2018;

“***Fiscal Year***” means the periods ending on the accounting reference date of the Company from time to time.

“***GAAP***” means generally accepted accounting principles applicable in the US.

“ ***IPO***” means 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 C Shareholder Majority only, less than $40,000,000.

“***Immediate Family Member***” means a child, stepchild, grandchild, parent, stepparent, grandparent, spouse, sibling, mother-in-law, father-in-law, sonin- law, daughter-in-law, brother-in-law, or sister-in-law, including, adoptive relationships, of a natural person referred to herein.

“***Investor***” means a holder of C Shares (or any A Shares which are held as a result of conversion or reclassification of such C Shares in accordance with the Articles) which, if such C Shares were converted and reclassified into A Shares, would constitute not less than 3% of the fully diluted share capital of the Company.

“***Joinder Agreement***” has the meaning set forth in Section 8.2.

“***Majority of the Board***” means (i) if the Board of Directors is comprised of more than one Director, the affirmative vote of a majority of the Directors then comprising the Board of Directors and (ii) if the Board of Directors is comprised of one Director, the vote of that Director.

“***Member***” means any Person holding Shares from time to time.

“***Person***” means any natural person, partnership, corporation, limited liability company, trust, estate, association, unincorporated organization or other entity or association.

“***Registrable Shares***” means, with respect to each Investor, a number of A Shares equal to the C Shares held by such Investor on [ ] May 2018 minus the number of A Shares that such Investor has previously registered pursuant to the terms of this agreement; provided, however, upon transfer other than an assignment pursuant to Section 10.3 hereof neither a C Share nor an A Share converted from a C Share shall constitute a Registrable Security.

“***Share***” means an A Share and/or a C Share.

**SECTION 2. Formation, Purpose, Term.**

2.1 **Name**. The business of the Company shall be conducted under the name “ MeiraGTx Holdings plc”.

2.2 **Purposes**. The Company is organized for the purpose of transacting any and all lawful business of an exempted company to the fullest extent permitted under the Act. Subject to the provisions of this Agreement and the Memorandum and Articles of Association of the Company, the Company shall have the power to do any and all acts and things necessary, appropriate, advisable or convenient for the furtherance and accomplishment of the purposes of the Company, including, without limitation, to engage in any kind of activity and to enter into and perform obligations of any kind necessary to or in connection with, or incidental to, the accomplishment of the purposes of the Company, so long as said activities and obligations may be lawfully engaged in or performed by a company under the Act.

2.3 **Powers**. The Company shall possess and may exercise all powers necessary, convenient or incidental to the conduct, promotion or attainment of the business purposes to the fullest extent provided in the Act and the Memorandum and Articles of Association of the Company.

2.4 **Registered Office**. The registered office of the Company shall be at Walkers Corporate Limited, Cayman Corporate Centre, 27 Hospital Road, George Town, Grand Cayman KY1-9008, Cayman Islands, or such other place as shall be determined by the Board of Directors.

2.5 **Organization Expenses**. The Company shall pay all expenses incurred in connection with the formation and incorporation of the Company. Such expenses shall include, without limitation, fees of legal counsel, filing and publication costs and other like expenses.

2.6 **Register of Members; Transfer**. Shares may, subject to the Act, be issued for such consideration as the Board of Directors may determine, subject to the other provisions of this Agreement and the Articles. The Company shall maintain at its registered office (or such other place as the Directors may determine in accordance with the Articles) a register of Members containing the names and addresses of the holders of record of Shares, in accordance with the requirements of the Act. Shares may only be transferred in accordance with the terms of this Agreement and the Articles and each such transfer shall be recorded in the books of the Company.

2.7 **Proposed IPO**. The Company and the Members agree and acknowledge that it is proposed to effect an IPO of the Company within such period as may be approved by the Board of Directors and accordingly the Members undertake to pass all resolutions and give all consents as may be reasonably required to effect such an IPO on terms that are consistent with the terms of this Agreement and the Articles, as may be recommended to be given by the investment bank(s) engaged by the Company to advise it in respect of such IPO. The Parties acknowledge and agree that:

(a) Members may be required to give appropriate warranties, representations, covenants, undertakings and indemnities in connection with the IPO;

(b) Members may be required to undertake to retain an appropriate shareholding in the Company for an appropriate period after the date of the IPO; and

(c) the Company shall, conditional on the IPO being effected, adopt new articles of association appropriate for a listed company, which will provide, inter alia, for a single class of shares which will rank pari passu in all respects.

**SECTION 3. Members; Share Rights**

3.1. Each Member shall have the rights and powers with respect to each Share registered in the name of such Member as set forth in this Agreement and in the Articles.

3.2 Reserved Matters. The following matters shall require the approval of a C Shareholder Majority (provided at least 20% of the aggregate C Shares in issue as at the Effective Date remain in issue) and each of the Shareholders undertakes to exercise its voting rights or refrain from exercising its voting rights in order to give effect to such matters:

(a) the authorization, creation or incurrence of any obligation to issue or issuance of any shares in the Company ranking senior to the C Shares with respect to voting rights, dividends, conversion, distributions upon liquidation of the Company or redemption rights;

(b) the effecting of a liquidation of the Company or a sale of the Company;

(c) the payment or declaration of any dividends or other distributions on the A Shares or redemption or repurchase of any shares by the Company, other than the repurchase of Shares from employees of the Company upon a termination of employment pursuant to an agreement to repurchase such Shares that is approved by the Board;

(d) the borrowing of any money in excess of $5,000,000 in the aggregate outside of the ordinary course and other than pursuant to debt facilities approved by the Board;

(e) the guaranteeing, whether direct or indirect, of the payment or performance of indebtedness of another party in excess of $5,000,000 in the aggregate;

(f) an increase in the number of shares in the capital of the Company, excluding the Company’s incentive plans up to a cap of 12.5% of the fully diluted share capital; and

(g) any deviation from the annual budget approved by the Board by more than ten percent (10%).

3.3

3.4 **Limitation on Liability**. No Member shall be liable for any debt, obligation or liability of the Company, whether arising in contract, tort or otherwise, except as provided by law or as specifically provided otherwise herein. All Persons dealing with the Company will have recourse solely to the assets of the Company for the payment of the debts, obligations or liabilities of the Company.

3.5 **Transactions Involving a Member or Affiliate of a Member**

All transactions, agreements or arrangements between (i) the Company or any of its subsidiaries on the one hand and (ii) any of the Company's Affiliates, a Member or any of such Member's Affiliates on the other, shall be at prices and on terms and conditions not less favorable to the Company and its subsidiaries than could be obtained on an arm's-length basis from unrelated third parties, as reasonably determined in good faith by a majority of the disinterested members of the Board of Directors.

3.6 **Confidentiality**.

(a) Company Confidential Information. None of the Members, any Director, or any of their respective representatives shall, without the prior written consent of the Company, divulge, disclose or make accessible to any other Person (other than its officers, directors, employees, agents, professional advisors and partners), or use for its own benefit in connection with matters unrelated to the Company, any Confidential Information (as herein defined), except (i) to potential purchasers of Shares when such potential purchasers have entered into a valid and binding confidentiality agreement that is no less restrictive than the terms contained herein, (ii) when required to do so by applicable law or regulations or by a court of competent jurisdiction, by any governmental agency having supervisory authority or by any administrative body or legislative body (including a committee thereof) with purported or apparent jurisdiction to order such Person to divulge, disclose or make accessible such information or (iii) to any Affiliate of such Person or accountant, legal counsel or other advisors (including any advisors and sub-advisors to the funds and accounts managed by such Person) of such Person that need to know such information in connection with such Members' or Directors' investment, obligations or duties with respect to the Company (such Persons, the "***Representatives***") (provided, with respect to this clause (iii), each such Representative agrees to comply with the provisions of this Section 3.6(a) with respect to such Confidential Information received by such Representative); notwithstanding anything in this Agreement to the contrary, the Company acknowledges that the Members' and their respective Representatives' businesses include the analysis of, and investment in, securities, instruments, businesses and assets and the review of the Confidential Information given to the Members and their respective Representatives inevitably will serve to give the Members and their respective

Representatives a deeper overall knowledge and understanding in a way that cannot be separated from the Members' or such Representatives' other knowledge. Accordingly, and without in any way limiting the Members' obligations under this Agreement, the Company agrees that this Agreement shall not restrict the Members' use of such overall, generalized knowledge and understanding retained in the unaided memory of individual personnel for the Members' own internal purposes, including the purchase, sale, consideration of, and decisions related to other investments. For purposes of this Agreement, "***Confidential Information***" shall mean non-public information concerning the Company's or any of its subsidiaries' financial data, strategic business plans, product development (or other proprietary product data), customer lists, customer information, information relating to governmental relations, discoveries, practices, processes, methods, marketing plans and other material non-public, proprietary and confidential information, that, in any case, is not otherwise generally available to the public and has not been disclosed by the Company and its subsidiaries to others not subject to confidentiality agreements. Notwithstanding anything to the contrary described herein, the parties hereto and each of their respective employees, representatives or other agents, are permitted to disclose to any and all Persons, without limitations of any kind, the tax treatment and tax structure of the transactions and all materials of any kind (including opinions or other tax analyses) that are or have been provided to such parties related to such tax treatment and tax structure; provided, however, that the foregoing permission to disclose the tax treatment and tax structure does not permit the disclosure of any information that is not relevant to understanding the tax treatment or tax structure of the transactions; provided, further, however, that the tax treatment and tax structure shall be kept confidential to the extent necessary to comply with federal, state or other applicable securities laws.

(b) Member Confidentiality. Neither the Company nor any of its representatives or Affiliates shall issue any press releases or other public or private disclosure using the name of any Member or any information provided by the Member in relation to its investment in the Company or any of its Affiliates (whether in connection with the Company or otherwise) without obtaining Member's prior written consent, nor may the Company release information provided by the Member to the Company's auditors, employees, representatives or other agents and the Member's name shall not appear in any financial statements which are distributed to anyone other than the other Members or the Company or its Affiliates, except, in each case, (i) to potential purchasers of Shares when such potential purchasers have entered into a valid and binding confidentiality agreement that is no less restrictive than the terms contained herein, (ii) when required to do so by applicable law or regulations or by a court of competent jurisdiction, by any governmental agency having supervisory authority or by any administrative body or legislative body (including a committee thereof) with purported or apparent jurisdiction to order such Person to divulge, disclose or make accessible such information or (iii to any Affiliate of such Person or accountant, legal counsel or other advisors of such Person.

3.7 **No Management by Members**. Except as expressly provided in this Agreement, no Member will have the right by virtue of such Member's membership to take part in or interfere in any manner with the management of the business and affairs of the Company or have any right or authority to act for or bind the Company.

3.8 **Meetings and Voting**.

(a) The Members shall have a meeting on such date and at such frequency as may be determined by the Board of Directors in their sole discretion for the purpose of conducting such business as may properly come before the meeting; provided, however that a meeting of the Members shall occur at least once every twelve (12) months. At any meeting of Members, only such business may be transacted as is related to the purpose or purposes set forth in the notice of such meeting. Except as otherwise provided herein, including, without limitation, with respect to the appointment of Board Members, the Members may take action at a properly called meeting with respect to any item of business by a vote of the Members having a majority of the voting rights underlying the Shares (including, in each case, a C Shareholder Majority), unless otherwise provided by any provision of applicable law, this Agreement or the Articles.

(b) Written notice of every meeting of Members shall be given not less than twenty (20) days before the date of the meeting to the Members entitled to vote, stating the place, date and hour thereof, and the purpose or purposes thereof.

(c) Any vote, consent or approval of the Members entitled to vote may be accomplished by written consent in lieu of a meeting signed by all of the Members that would be entitled to vote at such meeting.

3.9 **Capital Contributions**. None of the Members shall have any obligation to make any capital contributions to the Company in excess of paying such sums as are agreed to be paid up on each Share.

## SECTION 4. Management of the Company.

4.1 **Board of Directors**. The business of the Company will be managed by the Board of Directors.

(a) For so long as Kadmon Corporation, LLC holds not less than 10% of the issued Shares, it shall have the right, from time to time, by written notice to appoint one person to act as its nominated Director of the Company and to remove that Director from office and to appoint any person in his place (a "***Kadmon Director***"), and the other Members shall not vote their Shares so as to remove that Director from office save to the extent Kadmon Corporation, LLC ceases to hold 10% of the issued Shares. Neither of the directors appointed at Completion shall be the Kadmon Director.

(b) For so long as Perceptive Life Sciences Master Fund, Ltd., or its Affiliates, holds not less than 50% of the C Shares it owned on the Effective Date, it shall have the right, from time to time, by written notice to appoint one person to act as its nominated Director of the Company and to remove that Director from office and to appoint any person in his place (a "***Perceptive Director***"), and the other Members shall not vote their Shares so as to remove that Director from office save to the extent Perceptive Life Sciences Master Fund, Ltd., or its Affiliates ceases to hold 50% of the C Shares it owned on the Effective Date. Neither of the directors appointed at Completion shall be the Perceptive Director.

(c) Further Directors shall be appointed or removed in accordance with this Agreement, the Articles and the Act.

(d) The Board of Directors shall have full and exclusive authority, power and discretion to manage and control the business, affairs and properties of the Company, to make all decisions regarding those matters and to perform any and all other acts or activities customary or incident to the management of Company business, unless otherwise provided in the Act or this Agreement. Except as expressly provided herein, the vote of a Majority of the Board shall be required to approve or effect any action or transaction on behalf of the Company.

(e) The Directors as of the date hereof are Alexandria Forbes, Joel Marcus, Neil Mendoza, Keith Harris, Stuart Naylor, Thomas Shenk, Arnold J. Levine, Gregory S. Moss and Ellen Hukkelhoven (along with any Directors appointed from time to time, the "***Board Members***"). The number of Directors may be increased from time to time by resolution of the Board of Directors.

(f) Any Director may resign at any time. Such resignation shall be made in writing and shall take effect at the time specified therein, or if no time be specified, at the time of its receipt by the Company. The acceptance of a resignation shall not be necessary to make it effective, unless expressly so provided in the resignation.

(g) Save as provided in (a) and (b) above, any Director may be removed at any time by a majority vote of the other Directors.

(h) In the event of a vacancy on the Board of Directors due to the resignation or removal of any Director, such vacancy may only be filled by a majority vote of the Board of Directors. Any Director position to be filled by reason of an increase in the number of Directors may be filled by the Person selected by the vote of the Board of Directors.

(i) Each Director shall be required to devote such time to the affairs of the Company as the Board of Directors reasonably determines may be necessary or appropriate to manage and operate the Company.

(j) The Board of Directors may delegate all or part of its authority to committees of the Board or employees of the Company whom the Board of Directors may appoint from time to time, including, without limitation, employees possessing the titles of President, Vice President, Treasurer and Secretary.

(k) Each Director will be at liberty from time to time to make such disclosure to any Member who appointed him in relation to the Business or affairs of the Company as he thinks fit.

4.2 **Compensation of Board of Directors; Reimbursements**. The Directors may receive compensation for performing his/her duties as a member of the Board of Directors, in such amounts as are determined in good faith by the Board of Directors to be reasonable under the circumstances. A Director shall also be entitled to reimbursement of his/her reasonable out-of-pocket expenses in connection with the performance of such duties.

**SECTION 5. Accounting and Records.**

5.1 **Records and Accounting**. The books and records of the Company shall be kept, and the financial position and the results of its operations recorded, at the expense of the Company in accordance with the accounting methods elected to be followed by the Company which shall be on an accrual basis for financial reporting purposes and for income tax purposes. The books and records of the Company shall reflect all Company transactions and shall be appropriate and adequate for the Company's business. The Fiscal Year of the Company shall be the calendar year.

5.2 **Access to Accounting Records**. All books and records of the Company shall be maintained at the Company's principal place of business, and each Member, and the Member's duly authorized representative, shall have access to them at such office of the Company and the right to inspect and copy them at reasonable times for any purpose reasonably related to its interest in the Company.

5.3 **Accounting Decisions**. All decisions as to accounting matters shall be made by the Board of Directors.

5.4 **Income Tax Elections**. All decisions as to tax elections and accounting matters shall be made by the Board of Directors.

**<u>SECTION 6.</u>** **<u>Additional Members; Preemptive Rights</u>.**

**Additional Members**. In the event that the Board of Directors determines in good faith that additional capital is reasonably necessary, the Board of Directors may cause the Company to issue additional Shares to existing Members or third parties (and admit such third parties as Members), provided always that there is no obligation on any existing Member to contribute or invest further capital into the Company and such issue of Shares shall be in accordance with the Articles.

**<u>SECTION 7.</u>** **<u>Deposit and Use of Company Funds</u>.**

All capital contributed to the Company shall be made to or deposited in a separate Company account or accounts in such banks or other financial institutions as may be selected by the Board of Directors. Such account or accounts shall be maintained in the name of or for the benefit of the Company. All revenues, bank loans, proceeds and other receipts shall be deposited and maintained in such account or accounts, which may or may not bear interest, and all expenses, costs and similar items payable by the Company shall be paid from such accounts. The Company’s funds, including, but not limited to, Company revenue and the proceeds of any borrowing by the Company, may be invested as the Board of Directors deems advisable. Any interest or other income generated by such deposits or investments shall be considered part of the Company’s account. Company funds from any of the various sources mentioned above may be commingled with other Company funds, but not with the separate funds of any other Person, and may be withdrawn, expended and distributed as authorized by the terms and provisions of this Agreement.

**<u>SECTION 8.</u>** **<u>Transfer of Shares</u>.**

8.1 **Transfers**. The Directors shall only approve the registration of any transfer of Shares where such transfers are effected in accordance with the Articles.

8.2 Transfers following IPO. Upon the occurrence of an IPO, the Members will agree such restrictions on the disposal of their Shares or shares in any Affiliate of the Company for a period after the IPO, as are required by an underwriter in connection with the IPO.

8.3 **Admission to Membership**. Any Person that is not already a party to this Agreement who acquires any Shares shall, on or before the transfer or issuance to it of Shares (and as a condition thereto), sign and deliver to the Company a Joinder Agreement substantially in the form and on the terms of <u>Exhibit B</u> hereto (a “***Joinder Agreement***”), and shall thereby adhere and become a party to this Agreement.

**<u>SECTION 9. Warranties</u>.**

9.1 **Member Warranties**. Each Member (except that where such Member is incorporated, established resident and present outside of the United States of America such Member shall not warrant Section 9.1(a)) severally and not jointly hereby warrants to, and covenants and agrees with, the Company as follows:

(a) The Shares will be acquired for its own account (or for a separate account managed by such Member) for investment. It is not purchasing such securities with a view toward distribution in a manner which would require registration under the United States Securities Act of 1933, as amended (the "***Securities Act***"). Such Member recognizes that the Shares have not been registered under the Securities Act, in reliance upon an exemption from such registration and agrees that it will not sell, offer for sale, transfer, pledge or hypothecate its Shares, in whole or in part (i) in the absence of an effective registration statement covering such transfer, pledge or hypothecation, or if an exemption from registration is applicable, if reasonably requested by the Company, upon receipt by the Company of an opinion of counsel reasonably acceptable to the Company and its counsel, and (ii) except in compliance with all applicable provisions of this Agreement.

(b) Such Member's authorization, execution, delivery, and performance of this Agreement and any related agreements do not conflict with any other agreement or arrangement to which that Member is a party or by which it is bound.

(c) Such Member has all requisite power and authority and, with respect to Members who are individuals, legal capacity, to execute and deliver this Agreement, to perform its obligations under this Agreement, and to consummate the transactions contemplated by this Agreement. With respect to Members which are not individuals, the execution, delivery and performance of this Agreement by such Member have been duly authorized, and no other entity or stockholder action or proceeding on the part of such Member or such Member's stockholders is necessary to authorize the execution, delivery and performance of this Agreement. This Agreement has been duly executed and delivered by such Member and, assuming the due execution of this Agreement by each of the other Members party hereto, this Agreement constitutes, a valid and binding obligation of such Member, enforceable against such Member in accordance with its terms, except to the extent that such enforceability may be subject to, and limited by, applicable bankruptcy, insolvency, reorganization, moratorium, receivership and similar laws affecting the enforcement of creditors' rights generally, and general equitable principles.

**<u>SECTION 10.</u> <u>Miscellaneous</u>.**

10.1 **Notices**. All notices and other communications under this Agreement shall be in writing and shall be deemed given when (a) delivered by hand, (b) transmitted by telecopier (and confirmed by return facsimile) or (c) delivered, if sent by Express Mail, Federal Express or other express delivery service, or registered or certified mail, return receipt requested, to the addressee at the address for such Member on Exhibit A hereto (or to such other addresses or telecopier number as a party may specify by notice given to the other party pursuant to this provision).

10.2 **Amendments**; Waivers. Except as otherwise provided herein, this Agreement may be amended, modified, terminated, or waived in whole or in part (and either generally or in a particular instance, and either retroactively or prospectively) only with the prior written consent of the Company and Members holding a majority of the total voting rights of Members; provided, that any amendment to this Agreement that would disproportionately and adversely affect any Member (or group of Members) shall also require the written consent of each such Member so affected (or a majority of the Shares held by the group of Members so affected, if applicable); provided that any provision hereof may be waived by any waiving party on such party's own behalf, without the consent of any other party. Section 10.15 hereof may be amended, modified, revised or waived in whole or in part (and either generally or in a particular instance, and either retroactively or prospectively) only with the prior written consent of the Company and holders of a majority of Registrable Shares (including shares convertible into Registrable Shares) then outstanding and held by Investors. The Company shall give prompt notice of any amendment, modification or termination hereof or waiver hereunder to any party hereto that did not consent in writing to such amendment, modification, termination, or waiver.

10.3 **Binding Effect**; **Successors and Assigns**. The provisions of this Agreement and any amendment, termination modification or waiver hereto shall be binding upon and inure to the benefit of the parties hereto, their respective personal representatives, heirs, successors and permitted assigns; provided, however, that nothing contained in this Section 10.3 shall be construed to permit any attempted transfer which would be prohibited or void pursuant to any other provision of this Agreement. The rights under this Agreement may be assigned (but only with all related obligations) by a Member to a transferee of Shares (including Registrable Shares) that (i) is an Affiliate of a Member, (ii) is a Member's Immediate Family Member or trust for the benefit of an individual Member or one or more of such Member's Immediate Family Members; provided, however, that (x) the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee and the Registrable Shares with respect to which such rights are being transferred; and (y) such transferee agrees in a written instrument delivered to the Company to be bound by and subject to the terms and conditions of this Agreement. For the purposes of determining the number of shares of Registrable Shares held by a transferee, the holdings of a transferee (1) that is an Affiliate or shareholder of a Member; (2) who is a Member's Immediate Family Member; or (3) that is a trust for the benefit of an individual Member or such Member's Immediate Family Member shall be aggregated together and with those of the transferring Member; provided further that all transferees who would not qualify individually for assignment of rights shall, as a condition to the applicable transfer, establish a single attorney-in-fact for the purpose of exercising any rights, receiving notices, or taking any action under this Agreement.

10.4 **Counterparts**. This Agreement may be executed in any number of counterparts, each of which shall be deemed an original, but all of which shall constitute one and the same instrument.

10.5 **Headings**. All headings contained in this Agreement are inserted as a matter of convenience and for ease of reference only and shall not be considered in the construction or interpretation of any provision of this Agreement.

10.6 **Exhibits**. All exhibits annexed hereto are expressly made a part of this Agreement, as fully as though completely set forth herein, and all references to this Agreement herein or in any of such exhibits shall be deemed to refer to and include all such exhibits.

10.7 **Terms**. Common nouns and pronouns shall be deemed to refer to masculine, feminine, neuter, singular or plural, as the identity of the Person or Persons may require.

10.8 **Severability**. Each provision hereof is intended to be severable. If any term or provision is illegal or invalid for any reason whatsoever, such illegality or invalidity shall not affect the validity of the remainder of this Agreement.

10.9 **Entire Agreement**. This Agreement, including all exhibits hereto, constitutes the entire agreement of the parties hereto with respect to the matters hereof and supersedes any other prior oral and written understandings or agreements.

10.10 **Rights of Third Parties**.

(a) Any person to whom Shares have been properly transferred pursuant to the provisions of this Agreement and the Articles and who has entered into a Joinder Agreement which is acknowledged by the Company, may enforce against the parties the benefits and rights of this Agreement expressed to be in favour of the original shareholder from whom their Shares have been transferred subject to and in accordance with the provisions of the Contracts (Rights of Third Parties) Act 1999.

(b) Except as provided in this Section 10.10, a person who is not a party to this Agreement shall have no right under the Contracts (Rights of Third Parties) Act 1999 to enforce any term of this Agreement. This clause does not affect any right or remedy of any person which exists or is available otherwise than pursuant to that Act.

10.11 **Governing Law**.

(a) This Agreement and any dispute or claim arising out of or in connection with this Agreement, its subject matter or formation (including any non-contractual dispute or claim) ("***Dispute***") are governed by and shall be construed in accordance with English Law.

(b) Each party irrevocably agrees that the courts of England and Wales shall have exclusive jurisdiction to settle any Dispute.

(c) Each party irrevocably agrees that the courts of England and Wales are the most appropriate and convenient courts to settle Disputes and, accordingly, no party will argue to the contrary. Further, each party irrevocably agrees that a judgment in any legal action or proceedings brought in the courts of England and Wales in relation to a Dispute shall be conclusive and binding on the parties and may be enforced in the courts of any other jurisdiction.

10.12 **No Waiver**. No course of dealing between the Company and any Member, and no delay by the Company in exercising any right, power or remedy, shall operate as a waiver or otherwise prejudice the exercise by the Company of that right, power or remedy against that or any other Member.

10.13 **Termination**. Without prejudice to the accrued rights of any party, and except in respect of the provisions of Sections 3.6, 10.2, 10.10, 10.11, 10.13 and 10.15, this Agreement shall cease and determine on the earlier of:

(a) a Share Sale (as defined in the Articles) or an IPO; and

(b) with respect to the rights and obligations of any Member, such Member ceasing to hold Shares or ceasing to be the beneficial owner of Shares provided that such party has first complied with its obligations under the Articles in respect of the transfer of Shares and the transferee, if appropriate, has entered into a Joinder Agreement.

With respect to the provisions of Section 10.15, without prejudice to the accrued rights of any party, this Agreement shall cease upon the third anniversary of the IPO.

10.14 **Information Rights**. The Company shall deliver the following reports to each Member:

(a) as soon as available and in any event within forty-five (45) days after the end of each of the first three quarters of each fiscal year of the Company, consolidated and consolidating balance sheets of the Company and its subsidiaries as of the end of such period, and consolidated and consolidating statements of income and cash flows of the Company and its subsidiaries for the period then ended prepared in conformity with GAAP, except as otherwise noted therein, and subject to the absence of footnotes and to year-end adjustments; and

(b) as soon as available and in any event within ninety (90) days after the end of each fiscal year of the Company, a consolidated and consolidating balance sheet of the Company and its subsidiaries as of the end of such year, and consolidated and consolidating statements of income and cash flows of the Company and its subsidiaries for the year then ended prepared in conformity with GAAP, except as otherwise noted therein, together with an auditor's report thereon of a public accounting firm of established national reputation.

10.15 **Registration Rights.**

(a) If the Company proposes to register any of its A Shares under the Securities Act in connection with a public offering of such securities solely for cash (other than in: (i) a registration relating to the sale of securities to employees of the Company or a subsidiary pursuant to a stock option, stock purchase, or similar plan; (ii) a registration relating to an SEC Rule 145 transaction; (iii) a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Investor's Registrable Shares; (iv) a registration in which the only Shares being registered are A Shares issuable upon conversion of debt securities that are also being registered; or (v) an IPO (collectively, a "***Company Offering****")*, the Company shall, at such time, promptly give the Investors notice of such registration (the "***Registration Notice***"). Upon the request of any Investor given within twenty (20) days after the Registration Notice, the Company shall, subject to the paragraph below, cause to be registered the number of Registrable Shares that such Investor has requested to be included in such registration (the "***Investor Requested Shares"***). The Company shall have the right to terminate or withdraw any registration initiated by it under this Section 10.15 before the effective date of such registration, whether or not the Investor has elected to include its A Shares in such registration. The expenses (other than all underwriting discounts, selling commissions, and stock transfer taxes applicable to the sale of the Investor's A Shares, and fees and disbursements of counsel for the Investor) of such withdrawn registration shall be borne by the Company.

(b) In connection with any Company Offering involving an underwriting of shares of the Companypursuant to the paragraph above, the Company shall not be required to include any of the Investor's Registrable Shares in such underwriting unless the Investor accepts the terms of the underwriting as agreed upon between the Company and its underwriters, and then only in such quantity as the underwriters in their sole discretion determine will not jeopardize the success of the Company Offering. If the total number of securities, including the Investor's Registrable Shares requested to be included in such offering, exceeds the number of securities to be sold (including those contained in the Company Offering) that the underwriters in their reasonable discretion determine is compatible with the success of the Company Offering, then the Company shall be required to include in the offering only that number of such shares, which the underwriters and the Company in their sole discretion determine will not jeopardize the success of the Company Offering, with the Company Offering having priority over the sale of the Investor's Registrable Shares. Notwithstanding the foregoing in the event that it is not possible to include all the Investors Requested Shares in the offering, the number of the Investor Requested Shares included in the offering shall be reduced pro rata for each Investor based on the number of Registrable Shares held.

(c) The right of the Investor to request inclusion of the Investor's Registrable Shares in any registration pursuant to the paragraphs above shall terminate upon the earliest to occur of: (i) a deemed liquidation event (as defined in the Articles) and (ii) such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of all of the Investor's then Registrable Shares without limitation during a three-month period without registration.

IN WITNESS WHEREOF, the parties hereto have duly executed this Agreement as of 2018.

| | | |
|---|---|---|
| Executed as a deed, but not delivered until the date specified on this deed, by **MEIRAGTX HOLDINGS PLC** by an authorised signatory in the presence of a witness: | )<br>)<br>)<br>) | Signature ________________<br><br>Name (block capitals) ________________<br>Director |

Witness signature ________________

Witness name ________________
(block capitals)

Witness address ________________

________________

________________

**Exhibit 23.1**

**Consent of Independent Registered Public Accounting Firm**

We consent to the reference to our firm under the caption “Experts” and to the use of our report dated March 29, 2018 (except for Note 6, as to which the date is May 11, 2018) in Amendment No. 3 to the Registration Statement (Form S-1 No. 333-224914) and related Prospectus of MeiraGTx Holdings plc for the registration of its ordinary shares.

/s/ Ernst & Young LLP

Stamford, Connecticut

June 1, 2018