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

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2019
OR
☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to
Commission file number: 001-38520

MEIRAGTX HOLDINGS PLC

(Exact name of registrant as specified in its charter)

Cayman Islands (State or other jurisdiction of incorporation or organization)	**Not applicable** (I.R.S. Employer Identification No.)
450 East 29th Street, 14th Floor **New York, NY** (Address of principal executive offices)	**10016** (Zip Code)

(646) 860-7985
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of exchange on which registered
Ordinary Shares, $0.00003881 Nominal value	**MGTX**	**The Nasdaq Global Select Market**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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	☒
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

As of June 28, 2019, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's ordinary shares held by non-affiliates of the registrant was approximately $511,316,440 (based upon the closing sale price of the registrant's ordinary shares on that date on the Nasdaq Global Select Market).

As of March 8, 2020, the registrant had 36,817,916 ordinary shares outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2020 annual shareholder meeting to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2019 are incorporated herein by reference in Part III of this Annual Report on Form 10-K.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (the "Form 10-K") contains forward-looking statements that can involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Form 10-K, 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 Form 10-K 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 Form 10-K and are subject to a number of risks, uncertainties and assumptions described under the sections in this Form 10-K entitled "Item 1A. Risk Factors" and "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Form 10-K. 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. Thus, one should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements.

You should read this Form 10-K and the documents that we reference in this Form 10-K and have filed as exhibits to this Form 10-K, 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 Form 10-K, 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. These statements should not be relied upon as representing our views as of any date subsequent to the date of this Form 10-K.

BASIS OF PRESENTATION

On June 7, 2018, in connection with its initial public offering (the "IPO"), MeiraGTx Holdings plc, an exempted company incorporated under the laws of the Cayman Islands, acquired all the issued and outstanding ordinary shares of MeiraGTx Limited pursuant to a series of reorganization transactions. We refer to these events in this Form 10-K as the "Reorganization Transactions." Prior to the Reorganization Transactions, MeiraGTx Holdings plc had not conducted any operations and had nominal assets and liabilities.

Unless the context otherwise requires, references in this Form 10-K to "Meira," "we," "us", "our" or "the Company" refer to (i) MeiraGTx Limited and its subsidiaries prior to the Reorganization Transactions and (ii) MeiraGTx Holdings plc and its subsidiaries upon completion of the Reorganization Transactions, as applicable.

We have proprietary rights to trademarks, trade names and service marks appearing in this Form 10-K that are important to our business. Solely for convenience, the trademarks, trade names and service marks may appear in this Form 10-K 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 Form 10-K are the property of their respective owners.

INDUSTRY AND OTHER DATA

We obtained the industry, market and competitive position data in this Form 10-K 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.

PART I

ITEM 1. BUSINESS

Overview

We are a vertically integrated, clinical stage gene therapy company with six programs in clinical development 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 own and operate a flexible and scalable viral vector manufacturing facility that we expect can supply our current ophthalmology, neurodegenerative disease and salivary gland 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, or MHRA.

We intend to expand our manufacturing capabilities by building a second cGMP viral vector manufacturing facility and a cGMP plasmid production facility. We currently rely on third-party manufacturers for the plasmid used in the production of our product candidates. We are in the planning stages for our new facilities and we expect to begin construction in 2020. We believe that building a second viral vector manufacturing facility and bringing cGMP plasmid production in-house will provide greater flexibility and efficiency as we advance our product candidates through development, and should they be approved, commercial production.

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 expression 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 and the status of such product candidates as of March 1, 2020 is described below. We retain worldwide development and commercialization rights to all of our product candidates, with the exception of AAV-CNGB3, AAV-CNGA3 and AAV-RPGR, which are subject to a strategic Collaboration, Option and License Agreement (the “Collaboration Agreement”) that we executed with Janssen Pharmaceuticals, Inc. (“Janssen”), one of the Janssen Pharmaceutical Companies of Johnson & Johnson on January 30, 2019.

*Co-development program with Janssen Pharmaceuticals pursuant to a collaboration agreement.

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:

- 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;
- gene regulation—use of our proprietary RNA shape regulation cassette to switch gene therapy expression on and off with small molecules, potentially transforming gene therapy technology into a delivery mechanism for a broad array of biologic drugs; and
- inflammatory diseases—use of gene therapy technology for the local delivery of immunomodulatory therapeutics.

Our Ophthalmology Programs

Eye diseases are our first area of clinical focus and we aim to provide treatments with durable, long-term clinical benefit that will halt vision loss in patients. We currently have four Phase 1/2 clinical programs targeting IRDs, including AAV-CNGB3 and AAV-CNGA3 for the treatment of achromatopsia, or ACHM, related to mutations in *CNGB3* and *CNGA3*, respectively, AAV-RPGR for the treatment of X-linked retinitis pigmentosa related to mutations in *RPGR*, or XLRP-RPGR, and AAV-RPE65 for retinal dystrophy related to mutations in *RPE65*, or RPE65 deficiency. In addition to these four programs, our product candidate AAV-AIPL1 was manufactured and released for compassionate use under an MHRA specials license in the United Kingdom, or UK, to treat patients with Leber congenital amaurosis 4, or LCA4, caused by mutations in *AIPL1*. In addition to these clinical programs in IRDs, we have preclinical programs that apply novel approaches to both wet and dry AMD.

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 is needed 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.

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.

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.

AAV-RPGR for the Treatment of X-Linked Retinitis Pigmentosa Associated with Mutations in the RPGR Gene

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. 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. 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 (U.S.), Japan and Germany, France, Spain, Italy and the UK, or the EU5, with a little less than 50% of 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.

There are currently no approved treatments for XLRP.

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, retinal imaging and electrophysiological assessments. We believe access to this large population of XLRP-RPGR patients has enabled us to efficiently enroll appropriate patients into our XLRP clinical development program.

Since 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 the central region of the retina, including the macula and fovea, must be preserved to prevent the ultimate degeneration to blindness and to retain visual acuity. To this end, we aim to deliver AAV-RPGR to this central region of the retina.

We are conducting a Phase 1/2 clinical trial of AAV-RPGR in XLRP patients. AAV-RPGR 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.

In the dose escalation portion of the Phase 1/2 trial, we enrolled 13 patients, including 10 young adults and 3 children. After we completed dosing patients in the dose escalation portion of the study, we began enrolling patients in the randomized, controlled, extension portion of the Phase 1/2 trial. We expect data from this study to be reported in 2020.

The FDA has granted Fast Track and orphan drug designations to AAV-RPGR. The European Medicines Agency, or EMA, has granted Priority Medicines (PRIME) and orphan drug designations to AAV-RPGR.

AAV-RPE65 for the Treatment of RPE65-Associated Retinal Dystrophy

We are developing AAV-RPE65 for the treatment of retinal dystrophy associated with mutations in the *RPE65* gene. *RPE65*-associated retinal dystrophy causes rod photoreceptor dysfunction and impaired vision from birth. 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*-associated retinal dystrophy patients experience central vision loss progressing to complete blindness by early adulthood.

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 have developed a gene therapy candidate optimized for safety and potency for the treatment of *RPE65*-associated retinal dystrophy, AAV-RPE65. AAV-RPE65 is an AAV2/5 viral vector, in which a codon optimized *RPE65* gene is driven by a novel synthetic retinal pigment epithelium cell specific promoter.

The FDA recently approved the first gene treatment for *RPE65*-associated retinal dystrophy, Luxturna, a commercially available product developed by Spark Therapeutics, Inc., which was purchased by Roche. While *RPE65*-associated retinal dystrophy 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.

Clinical Development of AAV-RPE65

We have an ongoing natural history study in patients with RPE65-associated retinal dystrophy with approximately 30 patients enrolled that allows us to collect structural and functional data on prospectively defined endpoints, including functional tests, retinal imaging, and electrophysiological assessments.

Our Phase 1/2 clinical trial enrolled *RPE65*-associated retinal dystrophy patients in the UK and U.S. Dosing in the Phase 1/2 clinical trial was completed in June 2018. The primary endpoint of this open-label, dose-escalation clinical trial is safety. Secondary endpoints include the outcomes of a range of functional tests, detailed structural analysis of the retina and quality of life measures. A total of 15 patients were treated in this clinical trial, including nine adult patients in three dose escalation cohorts and six pediatric patients in the pediatric extension arm of the trial.

In May 2019, we announced positive topline safety and efficacy data from the Phase 1/2 trial of AAV-RPE65. Additional data from this study were presented at the Retina Subspecialty Day of the American Academy of Ophthalmology Annual Meeting in October 2019.

AAV-RPE65 met the study's primary endpoint of safety and tolerability. Additionally, AAV-RPE65 demonstrated statistically significant improvement across several secondary endpoints assessing clinical activity. Significant improvement in vision was demonstrated at six months after AAV-RPE65 treatment, as measured by assessments of vision-guided mobility, retinal sensitivity, visual acuity and contrast sensitivity. Larger improvements from baseline in functional vision were observed between treated and control eyes at lower light levels. We believe these outcomes address the core functional manifestation of *RPE65*-associated retinal dystrophy, which typically causes vision

impairment beginning in early childhood that is most pronounced in low-light conditions, and is consistent with the proposed mechanism of action of AAV-RPE65.

We intend to meet with regulatory agencies in 2020 to discuss the regulatory pathway forward for AAV-RPE65.

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.

AAV-CNGB3 and AAV-CNGA3 for the Treatment of Achromatopsia

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. 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. The *CNGB3* and *CNGA3* genes are the two most common genes that have been identified as causing ACHM, together accounting for up to 92% of ACHM cases, with *CNGB3* slightly more common than *CNGA3* in most geographic territories.

There are estimated to be approximately 12,000 patients with ACHM caused by mutations in *CNGB3* in the United States, Japan, and 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.

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.

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.

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, retinal imaging and electrophysiological assessments. We believe access to these ACHM patients has enabled us to efficiently enroll the most appropriate patients into our *CNGB3* and *CNGA3* Phase 1/2 clinical trials. 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 trials in a condensed timeframe.

Clinical Development of AAV-CNGB3 for the Treatment of ACHM Caused by Mutations in CNGB3

We have developed a product candidate, AAV-CNGB3 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 *CNGB3* 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.

We are conducting a Phase 1/2 clinical trial of AAV-CNGB3 in both adult and pediatric patients. In this trial, AAV-CNGB3 was 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. The primary endpoint of this open-label, dose-escalation clinical trial is safety. Secondary endpoints include the outcomes of a range of functional and structural assessments.

Dosing was completed in this clinical trial in May 2019. In the dose escalation portion of the trial, we treated 11 adults. We also treated 12 children in the pediatric expansion cohorts. Six months following treatment, patients can move 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.

Our gene therapy product candidate AAV-CNGB3 was granted orphan drug designation by the FDA and EMA, rare pediatric disease designation by the FDA for the treatment of achromatopsia caused by mutations in the *CNGB3* gene, and Fast Track designation by the FDA for the treatment of achromatopsia caused by *CNGB3* mutations. We were granted PRIME designation by the EMA in October 2018 based on data from the first adult treatment cohort along with preclinical data.

Clinical Development of AAV-CNGA3 for the Treatment of ACHM Caused by Mutations in CNGA3

We are also developing AAV-CNGA3 to treat ACHM caused by mutations in the *CNGA3* gene. We have designed a synthetic promoter to drive high levels of *CNGA3* expression specifically in cones because we believe a larger amount of *CNGA3* protein is required to restore cone function as compared to *CNGB3*. 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.

We initiated a Phase 1/2 dose escalation trial of AAV-CNGA3 in pediatric ACHM patients with mutations in *CNGA3* in the third quarter of 2019.

AAV-AIPL1 for the Treatment of LCA4

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.

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 the University College of London, or 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.

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

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 MHRA.

Manufacturing a special also imposes a five year record retention requirement 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.

Ophthalmology Preclinical Development Pipeline

We also have a preclinical IRD development pipeline focused on diseases caused by mutations in additional genes. 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.

One of these pre-clinical programs relates to neovascular age related macular degeneration, or wet AMD. We use 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.

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. There is no currently approved therapy that impacts 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.

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.

AAV-AQP1 for the Treatment of Radiation-Induced Grade 2/3 Xerostomia

Radiation induced xerostomia, or RIX, is a severe and debilitating long-term side effect of radiation treatment for head and neck cancer. 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. There are currently no FDA approved treatments 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.

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 clinical trial conducted by the NIH in patients with chronic grade 2 or 3 RIX. The trial was designed as a short-term dose escalation trial of a gene therapy 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 of AAV-AQP1 at the NIH 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. 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 three cohorts and are enrolling patients into the fourth dose escalation cohort. This clinical trial is being conducted in conjunction with the National Institute of Dental and Craniofacial Research at the United States National Institutes of Health, or the NIH, Dental Clinic.

In the third quarter of 2019, we also initiated a multi-site Phase 1/2 clinical trial of our product candidate AAV-AQP1 for the treatment of grade 2 or 3 RIX. We have completed treating patients in the first dose escalation cohort and we expect to continue to open additional sites and enroll patients in dose escalation cohorts throughout 2020. We expect to report initial data from this clinical trial in the second half of 2020.

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.

AAV-AQP1 for the Treatment of 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 are currently conducting IND-enabling studies of AAV-AQP1 for xerostomia caused by Sjogren's syndrome.

Our Neurodegenerative Disease Programs

Neurodegenerative diseases are our third area of focus. 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.

AAV-GAD for the Treatment of Parkinson's Disease

Our first target indication is Parkinson's disease, where we have Phase 2 clinical data from a successful randomized, double-blind, sham-controlled trial.

Affecting nearly one million Americans and 10 million worldwide, Parkinson's disease is the second-most common neurodegenerative disease after Alzheimer's disease and is the 14th-leading cause of death in the United States. It is associated with a progressive loss of motor control (e.g., shaking or tremor at rest and lack of facial expression), as

well as non-motor symptoms (e.g., depression and anxiety). There is no cure for Parkinson's disease and 60,000 new cases are diagnosed each year in the United States alone.

Our product candidate targeting Parkinson's disease, AAV-GAD, is designed to deliver the glutamic acid decarboxylase, or *GAD*, gene to the subthalamic nucleus in order to increase production of GABA, the primary inhibitory neurotransmitter in the human brain. GAD is the rate-limiting enzyme in the synthesis of GABA, therefore we believe that increasing subthalamic nucleus GAD expression through gene therapy has the potential to address the dysregulation of motor circuits and improve symptoms in Parkinson's disease patients without affecting other brain regions, which can be responsible for complications of existing therapies.

Clinical Development of AAV-GAD

In a blinded Phase 2 clinical trial of AAV-GAD in patients with medically refractory Parkinson's disease, 45 patients were randomized 1:1 to receive either AAV-GAD gene therapy delivered by injection into the subthalamic nucleus on both sides of the brain or bilateral sham surgery. Subjects were followed for one year and all results remained blinded until the final treated patient reached the 6-month primary endpoint. The trial met the primary endpoint, of six-month change from baseline in double-blind assessment of off-medication motor scores of the Unified Parkinson's Disease Rating Scale, or UPDRS. At the six-month endpoint, UPDRS score for the AAV-GAD group decreased by 8.1 points (SD 1.7, 23.1%; $p<0.0001$) and by 4.7 points in the sham group (1.5, 12.7%; $p=0.003$). The AAV-GAD group showed a significantly greater improvement from baseline in UPDRS scores compared with the sham group over the six-month course of the study (RMANOVA, $p=0.04$). An improvement in complications of medical therapy as measured by the UPDRS part 4 was observed in the AAV-GAD group at both six and 12 months. A significant decline in duration of disabling dyskinesia was observed only in the AAV-GAD treated patients.

AAV-GAD was reported to be well-tolerated, with no significant adverse events related to the therapy and no speech or cognitive complications observed. The results of the trial were published in the March 2011 issue of *The Lancet Neurology*, the August 2014 issue of the *Journal of Clinical Investigation* and the April 2017 issue of *JCI Insight*, building upon publications of the Phase 1 trial data in *The Lancet* and the *Proceedings of the National Academy of Sciences*. In addition, in research published in the November 28, 2018 issue of *Science Translational Medicine*, fifteen patients treated with AAV-GAD gene therapy were observed to have expressed a treatment-related reorganization of functional brain connectivity that was related to disease symptom improvement. These flurodeoxyglucose positron emission tomography analyses provided objective biological evidence of improvements in abnormal brain networks associated with Parkinson's disease following AAV-GAD gene therapy.

These results were observed in patients treated in both Phase 1 and Phase 2 studies. Blinded analyses showed significant improvements in abnormal thalamic metabolism, a key node in the movement circuitry, in the AAV-GAD treated patients. This pattern of brain network activity was not seen in untreated hemispheres or patients in the sham arm. Furthermore, a specific pattern of brain network activity was identified in those subjects with clinical improvements in the sham arm, which was different from the pattern observed in AAV-GAD responders.

We intend to manufacture cGMP AAV-GAD material at our manufacturing facility and submit an Investigational New Drug Application (IND) to the FDA in 2020. To date, we have not determined the regulatory pathway and any potential related development costs for our AAV-GAD gene therapy program for Parkinson's disease.

Neurodegenerative Disease Preclinical Development Pipeline

In addition to our clinical stage Parkinson's disease program, we continue to conduct research to develop our preclinical pipeline of gene therapy product candidates for the treatment of other serious diseases of the central nervous system, including AAV-UPF1 to address motor neuron death in ALS, and an Alzheimer's disease program focused on endosomal trafficking dysfunction. Each of these programs are directed towards the underlying cell biology that may be driving neurogeneration in these diseases.

ALS

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.

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.

Alzheimer's Disease

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.

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 Strengths

In addition to our three core therapeutic areas of focus, our six ongoing clinical development programs, and our broad pipeline of preclinical programs, we have 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 our current clinical and preclinical programs through regulatory approval and, should they be approved, provide sufficient capacity for their commercial production. We are expanding our manufacturing capabilities by building a second cGMP viral vector manufacturing facility and building our own cGMP plasmid production facility.

- **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 gland disorders and neurodegenerative diseases. We have six programs in clinical development, one program under a compassionate use specials license and a broad preclinical development pipeline.

- **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.

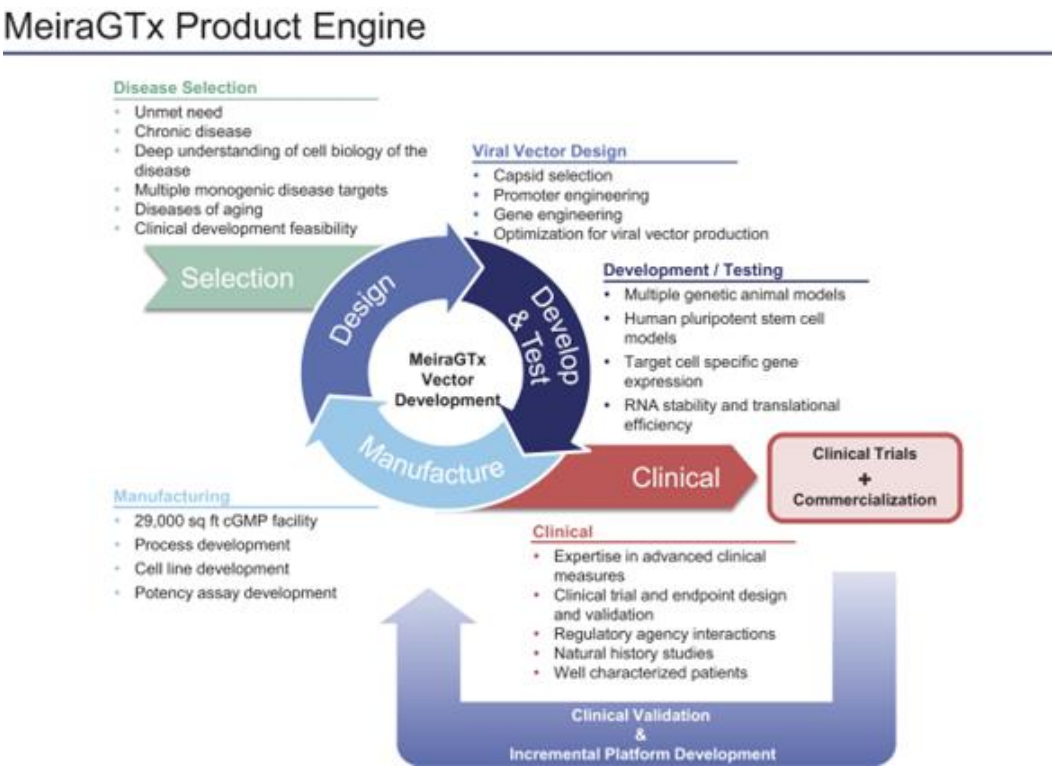
- **Natural History Study Data:** We sponsor ongoing prospective long-term natural history studies in IRDs that facilitate our ability to efficiently enroll our treatment studies, potentially reducing clinical trial timelines and providing insight into the appropriate endpoints for regulatory approval.

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;
- continue to advance the development of our preclinical pipeline product candidates;
- utilize our viral vector design and optimization capabilities to identify and develop new gene therapies for 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 regulatable product candidates; and
- continue to pursue and evaluate further strategic collaborations with additional biotechnology and pharmaceutical companies to leverage our capabilities, manufacturing capacity and proprietary gene regulation technology.

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



Gene Therapy Overview

Gene therapy uses a delivery vehicle, referred to as a vector, to insert a functionally active gene into cells in the body. The gene encodes a therapeutic protein that may block disease pathways or may enhance a deficient pathway. Gene therapy has been studied for over 50 years, with a variety of different viral vectors employed to deliver therapeutic genes. Since the first clinical study of therapeutic gene transfer in humans in 1990, thousands of 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, marketed by Spark Therapeutics, Inc. which was purchased by Roche, for treatment of *RPE65*-associated retinal dystrophy, and Zolgensma, marketed by AveXis, Inc., a Novartis company, for the treatment of spinal muscular atrophy, resulting in a growing acceptance of gene therapy technology as a potentially safe and effective therapeutic approach.

Our current programs use 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 in 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 IRD programs.

In addition to 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 in other types of diseases. 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 Competitive Advantage in IRDs: 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, or EU, 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.

For each of the natural history studies, baseline assessments are made upon enrollment, with follow up assessments at later time points. 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 that 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 also 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, among others, Moorfields Eye Hospital in London, the University of Michigan Kellogg Eye Center, Massachusetts Eye and Ear, the Medical College of Wisconsin & Froedtert Hospital and the Casey Eye Institute at the Oregon Health & Science University. These institutions and others where we have active relationships 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. They provide services with respect to our preclinical and clinical studies. Participants enrolled at the University of Michigan Kellogg Eye Center and Massachusetts Eye and Ear Hospital may 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.

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 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 *de-novo* mammalian riboswitches that we have observed respond to small molecules to switch genes on and off in mammalian cells and *in vivo* in mice. 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 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 small molecules we have the ability 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.

Using our proprietary technology, we have the ability to regulate multiple genes *in vitro and in vivo* in multiple tissue types using multiple small molecules. We are currently screening libraries to identify unique small molecule and aptamer pairs with the desired pharmacokinetic profiles for various therapeutic uses.

Our Manufacturing Capabilities

We own and operate a 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 MHRA, EMA and FDA standards.

We believe our facility can supply 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 vector 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 90 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 HEK-293 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 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.

We are also expanding our manufacturing capabilities by building a second cGMP viral vector manufacturing facility and building our own cGMP plasmid production facility. We currently rely on third-party manufacturers for the plasmid used in the production of our product candidates. We are in the planning stages for our new facilities and we expect to begin construction in 2020. We believe that building a second viral vector manufacturing facility and bringing cGMP plasmid production in-house will provide greater flexibility and efficiency as we advance our product candidates through development, and should they be approved, commercial production. We anticipate that the plasmid production facility will be operational by the end of 2020 and expect to initiate construction of the vital vector facility in mid-2020.

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 Biogen Inc. and a program AGTC is running to treat XLRP, as well as Luxturna, marketed by Spark Therapeutics, Inc. which was purchased by Roche, and has been approved to treat *RPE65*-associated retinal dystrophy. 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, as well as gene therapy product candidates being developed for the treatment of Parkinson's disease, including those being developed by Voyager Therapeutics, Inc., Prevail Therapeutics, Inc. and Axovant Sciences Ltd.

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 December 31, 2019, we own, co-own, have an exclusive license or co-exclusive license under, or an exclusive option to license 88 United States and foreign issued or allowed patents and 244 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 is 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 one granted patent in the United States and 22 pending patent applications with claims directed to compositions of matter and methods of use in the United States, Europe, Australia, Brazil, Canada, China, Hong Kong, Japan, Egypt, India, 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 second patent family includes 22 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, Hong Kong, 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, 2037, not including any patent term adjustments that may extend the patent term in certain jurisdictions.

The third patent family includes 22 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, Hong Kong, 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, 2037, not including any patent term adjustments that may extend the patent term in certain jurisdictions.

The fourth patent family includes 22 pending patent applications with claims directed to compositions of matter and methods of use in the United States, Europe, Australia, Canada, China, Hong Kong, 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 August 3, 2037, not including any patent term adjustments that may extend the patent term in certain jurisdictions.

The fifth patent family includes 21 pending patent applications relating to different gene regulation platform technologies 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. An additional filing in Hong Kong will be made in due course. Patents issued from this family are expected to expire on March 2, 2038, not including any patent term adjustments that may extend the patent term in certain jurisdictions.

The sixth patent family includes 21 pending patent applications relating to different gene regulation platform technologies 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. An additional filing in Hong Kong will be made in due course. Patents issued from this family are expected to expire on February 21, 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 UCL Business, Plc ("UCLB"), Brandeis University ("Brandeis") and the National Institute of Dental and Craniofacial Research ("NIDCR").

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 49 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 18 pending patent applications in the United States, Europe, Australia, Canada, China, Hong Kong, 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 into United States and international patent filings in due course. Patents issued from this family are expected to expire in January 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 one allowed patent application in the United States and six pending applications in the United States, Europe, Canada, China, and Japan (two applications). 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 25 pending applications in the United States, Europe, Australia, Canada, China, Hong Kong (two applications), 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 19, 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.

National Institute of Dental and Craniofacial Research

The exclusively licensed NIDCR portfolio includes one patent family with claims directed to compositions of matter and methods of use relating to our Sjogren's Syndrome gene therapy program. This patent family includes 16 issued or allowed patents in the United States, Canada, Australia, Austria, Belgium, Denmark, France, Germany, Ireland,

Italy, Netherlands, Norway, Spain, Sweden and United Kingdom and one pending patent application in the United States. Patents issued from this family are expected to expire August 30, 2033, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

License Agreements

License Agreements with UCLB

We previously entered into several license agreements with UCLB, covering the following inherited retinal disease programs: (a) ACHM caused by mutations in CNGB3; (b) ACHM caused by mutations in CNGA3; (c) XLRP; and (d) RPE65-mediated IRD (together, the "Licensed Gene Therapy Programs"). The terms of these license agreements were set forth in (i) the license agreement, dated February 4, 2015, as amended, between Athena Vision Ltd. And UCLB (the "First UCLB License Agreement"); (ii) the license agreements, dated July 29, 2017, as amended, between MeiraGTx UK II Limited and UCL Business, Plc (the "Second UCLB License Agreement"); and (iii) the license agreement, dated March 15, 2018, among MeiraGTx Limited, MeiraGTx UK II Limited and UCL Business Plc (the "Third UCLB License Agreement" and, collectively, the "prior UCLB license agreements"). In January and February 2019, we amended and restated the prior UCLB license agreements to establish new standalone license agreement (each, a "Stand-Alone UCLB Agreement") for each of the Licensed Gene Therapy Programs. We have removed from each of the Stand-alone Agreements our obligation to pay UCLB a share of certain sublicensing revenues as was provided under the First UCLB License Agreement and have aligned the material terms of the Stand-Alone Agreements to track those under the Third UCLB License Agreement as previously disclosed and a summary of which is set forth below as is now reflected in each of the Stand-Alone Agreements.

Under the terms of the Third UCLB License Agreement, we paid an initial upfront payment of £6,994, and issued to UCLB £100,000 of our ordinary shares. Under the Stand-Alone Agreement related to CNGB3, we paid UCLB an upfront payment of £1.5 million and issued £1.5 million of our ordinary shares.

Under each of the Stand-Alone UCLB Agreements, UCLB granted us an exclusive, worldwide, and sublicensable license under certain intellectual property rights controlled by UCLB relating to one of the Licensed Gene Therapy Programs to develop and commercialize licensed products in a relevant field of gene therapy. We must use diligent efforts to develop and commercialize the licensed products.

Under the terms of each Stand-Alone UCLB Agreement, we are required to pay UCLB sales milestone payments of up to a total of £39.8 million in the aggregate and an annual management fee of £50 thousand until certain royalty payments have been paid. Additionally, pursuant to the Stand-Alone UCLB Agreement related to CNGB3, we paid UCLB an upfront payment of £1.5 million and issued £1.5 million of the Company's ordinary shares.

Commencing on the first commercial sale of licensed products under each Stand-Alone UCLB Agreement, we must make low single-digit percentage royalty payments to UCLB on net sales of such products. Our royalty obligations under each 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.

Each Stand-Alone UCLB Agreement will remain in effect on a country-by-country basis until the expiration of the last payment obligation in such country. Each Stand-Alone 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 (or for 14 days in the case of breaches related to payment obligations), (b) by either party for the other party's insolvency, (c) immediately by UCLB if we are in persistent breach of the 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), 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. Each Stand-Alone 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. We require 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 United States.

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.

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 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. The FDA has also published guidance documents regarding the development of gene therapy products for retinal disorders and rare diseases.

To date, the FDA has approved four human gene therapy products for sale, 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. The FDA has also published guidance documents regarding the development of gene therapy products for retinal disorders and rare diseases.

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 studies, 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. 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 human clinical trials of cells containing recombinant or synthetic nucleic acid molecules, including human gene transfer studies, had historically been subject to review by the Recombinant DNA

Advisory Committee, or RAC, pursuant to the National Institutes of Health's Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. On August 17, 2018, the NIH issued a notice in the Federal Register and issued a public statement proposing changes to the oversight framework for gene therapy trials, including changes to the applicable NIH Guidelines to modify the roles and responsibilities of the RAC with respect to human clinical trials of gene therapy products, and requesting public comment on its proposed modifications. During the public comment period, which closed October 16, 2018, the NIH has announced that it will no longer accept new human gene transfer protocols for review as a part of the protocol registration process or convene the RAC to review individual clinical protocols. These trials will remain subject to the FDA's oversight and other clinical trial regulations, and oversight at the local level will continue as set forth in the NIH Guidelines. Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to the public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being 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.

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, enacted in 2012, 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, 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 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, integrity oversight and reporting obligations to resolve allegations of non-compliance 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 Patient Protection and Affordable Care Act, or 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, Congressional and executive branch challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, 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. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. While the Texas U.S. District Court Judge, as well as the Trump administration and the Centers for Medicare & Medicaid Services, or CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the law. 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, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. On January 31, 2019, the HHS Office of Inspector General proposed modifications to U.S. federal Anti-Kickback Statute safe harbors which, among other things, will affect rebates paid by manufacturers to Medicare Part D plans, the purpose of which is to further reduce the cost of drug products to consumers. 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.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

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 2021, 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 advanced therapy medicinal products, or 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 a Marketing Authorization Application, or 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 opinion is 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: (i) in 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 which 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 MHRA.

Manufacturing a special also imposes a five year record retention requirement 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.

Privacy and Data Protection Laws

We are also subject to laws and regulations in non-U.S. countries covering data privacy and the protection of health-related and other personal information. EU member states and other jurisdictions have adopted data protection laws and regulations, which impose significant compliance obligations. Laws and regulations in these jurisdictions apply broadly to the collection, use, storage, disclosure, processing and security of personal information that identifies or may be used to identify an individual, such as names, contact information, and sensitive personal data such as health data. These laws and regulations are subject to frequent revisions and differing interpretations, and have generally become more stringent over time.

The General Data Protection Regulation, or GDPR, is a European framework law which imposes many requirements for controllers and processors of personal data, including, for example, higher standards for obtaining consent from individuals, if this is required, to process their personal data, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention and secondary use of personal data, increased requirements pertaining to health data and pseudonymised (i.e., key-coded) data and additional obligations when we contract third-party processors in connection with the processing of personal data. The GDPR allows EU member states to make additional laws and regulations further regulating the processing of genetic, biometric or health data. Failure to comply with the requirements of GDPR and the applicable national data protection laws of the EU member states may result in fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties and may expose us to compensation claims from affected individuals.

The UK formally withdrew from the EU on January 31, 2020 and entered into a transition period that is scheduled to end on December 31, 2020. During the transition period, the status quo is maintained and the UK and the EU will continue to negotiate their future trading and immigration arrangements, and other aspects of their relationship. The UK's Data Protection Act 2018, or DPA2018, governs the UK's privacy regime and will continue to do so during and after the transition period. The GDPR will form part of UK domestic law as "retained EU law" as a result of the EU (Withdrawal) Act 2018, with certain amendments made to it and also to the DPA 2018 and the UK Privacy and Electronic Communications (EC Directive) Regulations 2003 under the (draft) Data Protection, Privacy and Electronic Communications (Amendments etc.) (EU Exit) Regulations 2019, which are intended to come into force after the transition period. Accordingly, the terms of the GDPR, and its significant penalties, will continue to apply during and after the transition period. At time of writing, it is unlikely that the UK will be granted adequacy by the European Commission (which would allow personal data to flow freely from the EU to the UK). If the UK is not granted adequacy, it will become a "third country" under the GDPR and data export mechanisms, such as Standard Contractual Clauses approved by the European Commission, may need to be put in place to govern the transfer of personal data from the EU to the UK.

Employees

As of December 31, 2019, we had 157 employees, all of which are full-time employees. 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.

Corporate Information

MeiraGTx Holdings plc was formed on May 1, 2018 under the laws of the Cayman Islands. Our predecessor, MeiraGTx Limited, a limited company under the laws of England and Wales, was formed on March 20, 2015. In connection with our IPO, we reorganized whereby MeiraGTx Limited became a wholly owned subsidiary of MeiraGTx Holdings plc.

Available Information

Our website can be found at *http://www.meiragtx.com*. From time to time, we may use our website as a channel of distribution of material company information. Financial and other material information is routinely posted and accessible under the Investors and Media section of our website at *http://www.meiragtx.com*.

We file annual, quarterly and current reports, proxy statements and other information with the U.S. Securities and Exchange Commission ("SEC"). Our SEC filings are available to the public over the Internet at the SEC's website at *http://www.sec.gov*. Our SEC filings are also available without charge under the Investors and Media section of our website at *http://www.meiragtx.com*. We make this information available on our website as soon as reasonably practicable after we electronically file such information with, or furnish it to, the SEC. Our website and the information contained on or connected to that site are not incorporated into this Form 10-K.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should consider carefully the risks described below, together with the other information included or incorporated by reference in this Form 10-K. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

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. 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 $54.8 million and $82.9 million for the years ended December 31, 2019 and December 31, 2018, respectively. As of December 31, 2019, we had an accumulated deficit of approximately $203.0 million. Since our inception, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facilities 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, developing our business plans, raising capital, and providing general and administrative support for these operations. We have not yet demonstrated an ability to successfully complete 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, development and manufacturing 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 as we operate as a public company and add clinical, scientific, operational, financial, compliance and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

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 (the "FDA"), European Medicines Agency (the "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 for the foreseeable future. These net losses 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, 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, we expect to continue to incur costs associated with operating as a public company. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our product candidate development efforts. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate certain of our research and development programs.

Our operations have consumed significant amounts of cash since inception. As of December 31, 2019, our cash and cash equivalents were $227.4 million. Based on our cash and cash equivalents at December 31, 2019 and the research funding we expect to receive under the Collaboration and License Agreement, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into 2022. 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 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 X-linked retinitis pigmentosa product candidate, AAV-RPGR, for our *CNGB3* achromatopsia gene therapy product candidate, AAV-CNGB3, for our *CNGA3* achromatopsia gene therapy product candidate, AAV-CNGA3,

for our *RPE65*-associated retinal dystrophy product candidate, AAV-RPE65, for our radiation induced xerostomia product candidate, AAV-AQP1, and to continue to conduct our ongoing natural history studies for inherited retinal diseases, or IRDs;

- the initiation of Phase 1/2 clinical trials for our product candidate for the treatment of ALS, AAV-UPF1, and for our product candidate for the treatment of xerostomia associated with Sjogren's syndrome, AAV-AQP1;
- ongoing discussions with regulatory agencies and potential subsequent initiation of future clinical trials for our product candidate for the treatment of Parkinson's disease, AAV-GAD;
- 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 facilities and activities;
- the cost of making royalty, milestone or other payments under current and any future in-license agreements;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;
- the extent to which we in-license or acquire rights to other products, product candidates 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, which are still in development, and if none of them receive regulatory approval or are successfully commercialized, our business may be harmed.

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 our product candidates. We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We have invested and expect to continue to invest a meaningful portion of our efforts and expenditures over the next few years in the development of AAV-RPGR, AAV-GAD, AAV-CNGB3, AAV-CNGA3, AAV-RPE65 and AAV-AQP1 (the "Most Advanced Product Candidates"), 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. While we have entered into a Collaboration and License Agreement with Janssen with respect to AAV-CNGB3, AAV-CNGA3 and AAV-RPGR, pursuant to which we received a $100 million upfront payment and will also receive funding for certain research, manufacturing, clinical development and commercialization costs, potential additional milestone payments upon the achievement of such milestones and royalties on future net sales of products, there can be no assurance that these three product candidates will be successfully developed and commercialized by us and Janssen. Accordingly, our business currently depends heavily on the successful development, regulatory approval and commercialization of our Most Advanced Product Candidates, which may never occur. We cannot be certain that our Most Advanced Product Candidates 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 our Most Advanced Product Candidates from the FDA, EMA or other regulatory bodies, we cannot be certain that our product candidates will be successfully commercialized by us or our collaborators, 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 our Most Advanced Product Candidates in the United States until they receive approval of a biologics license application, or BLA, from the FDA, we cannot market them in the European Union until we receive approval for a Marketing Authorization Application, or MAA, from the EMA, and we cannot market them in other countries until we receive any other required regulatory approval in those countries.

AAV-GAD, AAV-RPGR, AAV-CNGB3, AAV-CNGA3, 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 our

Most Advanced Product Candidates 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 may be 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.

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 control 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 a few product candidates 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 animal models will exist for some of the diseases we expect to pursue, 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, or IV, 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 current or future manufacturing facilities 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.

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, and/or an institutional review board, or IRB, which are local institutional committees or boards, as applicable, that review, approve and oversee basic and clinical research conducted at the institution participating in the clinical trial.

In Europe, 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, can take many years to complete and is 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, the EMA or other 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, EMA or other 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 development programs required for the approval of any of our product candidates. Although we have completed one Phase 1/2 clinical trial and are currently conducting several other ongoing Phase 1/2 clinical trials, we may experience delays in conducting any clinical trials and we do not know whether our ongoing and future 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 contract research organizations, or 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, CROs, 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 our product candidates 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;
- business interruptions resulting from geopolitical actions, including war and terrorism, or a widespread health emergency, such as the recent outbreak of a novel strain of coronavirus named COVID-19, or natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability;
- 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 they 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.

Our Most Advanced Product Candidates 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 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, or supporting the information, in our SEC filings and other materials should be viewed with caution. Further, the data and statistical information included, or supporting the information, in our SEC filings and other materials, 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 patients' 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 certain regulatory authority designations that may expedite the development or regulatory review of certain of our product candidates, in the future we may seek and fail to obtain access to such designations for other of our current or potential 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 the 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 August 2018, AAV-CNGB3 was designated a Fast Track program by the FDA for the treatment of achromatopsia caused by *CNGB3* mutations to improve visual function.

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.

Such regulatory designations are within the discretion of the FDA, EMA and other regulatory authorities. Accordingly, even if we believe one of our product candidates meets the criteria for such regulatory programs designed to accelerate the review and approval of new drugs and we seek such designations, the FDA, EMA or other applicable regulatory authority 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 such regulatory designations will meet the regulatory authority's expectations. In any event, the receipt of such regulatory designations for a product candidate may not result in a faster development process, review, or approval compared to product candidates considered for approval under conventional regulatory procedures and does not assure ultimate approval by the regulatory authorities. In addition, even if additional product candidates are granted such regulatory designations, the regulatory authority may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for review or approval will not be shortened.

We have received orphan drug designation from the FDA and EMA for AAV-CNGB3, AAV-CNGA3, AAV-RPE65, AAV-RPGR, AAV-AIPL1 and from the 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 principal molecular structural features, in the case of a biologic, 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 EMA for AAV-CNGB3 for the treatment of achromatopsia caused by mutations in the *CNGB3* gene, for AAV-CNGA3 for the treatment of achromatopsia due to autosomal-recessive *CNGA3* gene mutations, for AAV-RPE65 for the treatment of Leber congenital amaurosis, for AAV-RPGR for the treatment of retinitis pigmentosa and for AAV-AIPL1 for the treatment of inherited retinal 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 may seek orphan drug designation for other current and future product candidates in the future. 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 can subsequently approve products with the same principal molecular structural features, in the case of a biologic, for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Likewise, in the European Union, the EMA can approve a similar drug for the same therapeutic indication, if it concludes that the later drug is safer, more effective or clinically superior. 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. 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 and are in the planning stages of expanding our manufacturing capabilities, including building a second viral vector facility as well as a cGMP plasmid production facility. However, if we experience slowdowns or problems with our completed facility or the construction of our new facilities 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 of 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, or other issues with the manufacturing process, 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. In addition, our manufacturing process is complex, and the manufacturing batch cycle period can be several weeks long. Each batch cycle may not yield planned quantities or meet the required standards. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates, or other issues with our manufacturing process, 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.

Expanding our manufacturing capacity will be costly and we may be unsuccessful in doing so in a timely manner, which could delay our current and future clinical development programs, or delay the commercialization of our product candidates.

In addition to our existing manufacturing facility in London, United Kingdom, we may lease, operate, purchase, or construct additional facilities to conduct expanded manufacturing or other related activities in the future. We are in the planning stages of expanding our manufacturing capabilities to build a second viral vector facility as well as a cGMP plasmid production facility. Expanding our manufacturing capacity to produce the preclinical, clinical and commercial supply of our products will require substantial additional expenditures, time, and various regulatory approvals and permits. Further, we will need to hire and train significant numbers of employees and managerial personnel to staff our expanding manufacturing and supply chain operations. Start-up costs can be large, and scale-up entails significant risks related to process development and manufacturing yields. In addition, we may face difficulties or delays in developing or acquiring the necessary production equipment and technology to manufacture sufficient quantities of our product candidates for use in clinical trials and, should they be approved, to supply the commercial market at reasonable costs and in compliance with applicable regulatory requirements.

The FDA, the EMA and other foreign regulatory authorities must determine that our existing and any expanded manufacturing facilities comply, or continue to comply, with cGMP requirements for both clinical and commercial production and license them, or continue to license them, accordingly, and such facilities must also comply with applicable environmental, safety, and other governmental permitting requirements. We may not successfully expand or establish sufficient manufacturing capabilities or manufacture our products economically or in compliance with cGMP and other regulatory requirements, and we and our collaborators may not be able to build or procure additional capacity in the required timeframe to meet the requirements of our clinical programs or to meet commercial demand for our product candidates if they receive regulatory approval. This could also delay or require us to discontinue one or more of our clinical development programs or could interfere with our efforts to successfully commercialize our products. As a result, our business, prospects, operating results, and financial condition could be materially harmed.

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 marketed by Roche.

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 mutagenesis.

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 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 and / or our Collaboration and License Agreement partner obtain FDA or EMA approval for AAV-GAD, AAV-RPGR, AAV-CNGB3, AAV-CNGA3, 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 one or more 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. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. 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.

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;
- 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 & Medicaid 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, Congressional and executive branch challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, the Tax Cuts and Jobs Act of 2017, or the Tax Act, 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". Additionally, on December 14, 2018, a U.S. District Court Judge in Texas ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act.

On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how these decisions, subsequent appeals, if any, and other efforts to challenge, repeal or replace the ACA will impact the law or 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 2029 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 2020 contains further drug price control measures that could be enacted during the 2020 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. 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.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

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;

- 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;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain health care professionals (beginning in 2022), 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; and state and local laws that require the registration of pharmaceutical sales representatives; 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 government regulation and other legal obligations relating to privacy and data protection. Compliance with these requirements is complex and costly. Failure to comply could materially harm our business.

We are subject to statutes concerning data privacy and security, including HIPAA and the EU's General Data Protection Regulation, or GDPR. These and other regulatory frameworks are evolving rapidly as new rules are enacted and existing ones updated and made more stringent.

In the U.S., HIPAA imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon "covered entities" (health plans, health care clearinghouses and certain health care providers), and their respective business associates, individuals or entities that create, received, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HIPAA mandates the reporting of certain breaches of health information to HHS, affected individuals and if the breach is large enough, the media. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Even when HIPAA does not apply, according to the Federal Trade Commission or the FTC, failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 U.S.C § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The FTC's guidance for appropriately securing consumers' personal information is similar to what is required by the HIPAA security regulation.

In addition, certain state laws govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. For example, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the U.S. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA, which went into effect on January 1, 2020, requires covered companies to provide new disclosures to California consumers, and provides such consumers new ways to opt-out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. Some observers have noted that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business.

The GDPR applies to any company established in the EU as well as any company outside the EU that processes personal data in connection with the offering of goods or services to individuals in the EU or the monitoring of their behavior (including in the context of clinical trials). The GDPR imposes many requirements for controllers and processors of personal data, including, for example, higher standards for obtaining consent from individuals if this is required to process their personal data, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention and secondary use of personal data, increased requirements pertaining to health data and pseudonymised (i.e., key-coded) data and additional obligations when we contract third-party processors in connection with the processing of personal data. The GDPR allows EU member states to make additional laws and regulations further regulating the processing of genetic, biometric or health data. Failure to comply with the requirements of GDPR and the applicable national data protection laws of the EU member states may result in fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the

preceding financial year, whichever is higher, and other administrative penalties and may expose us to compensation claims from affected individuals.

The UK formally withdrew from the EU on January 31, 2020 and entered into a transition period that is scheduled to end on December 31, 2020. During the transition period, the status quo is maintained and the UK and the EU will negotiate their future customs and trading arrangements, and other aspects of their relationship. The UK's Data Protection Act 2018, or DPA2018, governs the UK's privacy regime and will continue to do so during and after the transition period. The GDPR will form part of UK domestic law as "retained EU law" as a result of the EU (Withdrawal) Act 2018, with certain amendments made to it and also to the DPA2018 and the UK Privacy and Electronic Communications (EC Directive) Regulations 2003 under the (draft) Data Protection, Privacy and Electronic Communications (Amendments etc.) (EU Exit) Regulations 2019, which are intended to come into force after the transition period. Accordingly, the terms of the GDPR, and its significant penalties, will continue to apply in the UK during and after the transition period. At time of writing, it is unlikely that the UK will be granted adequacy by the European Commission (which would allow personal data to flow freely from the EU to the UK). If the UK is not granted adequacy, it will become a "third country" under the GDPR and data export mechanisms, such as Standard Contractual Clauses approved by the European Commission, may need to be put in place to safeguard the transfer of personal data from the EU to the UK.

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 UK 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 UK and the U.S., 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 UK, 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 have established internal controls to detect and prevent violations of applicable anti-corruption laws 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 may 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. The FDA recently approved the first gene treatment for RPE65-associated retinal disease, Luxturna, a commercially available product developed by Spark Therapeutics, Inc., which was purchased by Roche. There are a number of other companies developing ocular gene therapy products, including Applied Genetic Technologies Corporation and Biogen, Inc. There are a number of companies developing gene therapy products for neurodegenerative diseases, including Voyager Therapeutics, Inc., Axovant Gene Therapies Ltd. and Prevail 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, or protein 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 enrollment in 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 these product candidates 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 or we may seek collaborative arrangements or external funding to commercialize our product candidates. For example, Janssen will be solely responsible for the commercialization of AAV-RPGR, AAV-CNGB3 and AAV-CNGA3 pursuant to our Collaboration and License Agreement with them. With respect to our other current and future product candidates, we would expect to build a focused sales, distribution and marketing infrastructure to market our product candidates in the United States and European Union, if approved, or seek to enter into collaborative relationships for such capabilities. 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 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-GAD, AAV-RPE65, AAV-AQP1 or other future gene therapy programs, if approved,

for the United States and/or certain markets overseas; however, there can be no assurance 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 or maintain a collaborative relationship for the commercialization of our product candidates, we may be forced to delay potential commercialization or reduce the scope of our sales or marketing activities. 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 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 or maintain adequate sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates 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 any of our products are commercialized outside of the United States or the European Union, a variety of risks associated with international operations could adversely affect our business.

If any of our products are approved for commercialization, we have entered into, and intend to enter into, agreements with third parties to market them in certain jurisdictions outside the United States and the European Union, such as under our Collaboration and License Agreement with Janssen. We expect that we and our third-party collaborators 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 widespread health emergency, such as the recent outbreak of a novel strain of coronavirus name COVID-19, 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 FCPA, the Bribery Act 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 and we may rely on other third parties to help us establish our international commercialization operations. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by individual countries in Europe with which we and our third-party collaborators 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 by the FDA. 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 the other company's 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.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, 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 licensed, 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.

If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

Risks Related to Our Dependence on Third Parties

If our 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 produce our product candidates in our cGMP viral vector manufacturing facility completed in early 2018 and are in the planning stages of expanding our manufacturing capabilities, including building a second viral vector facility as well as a cGMP plasmid production facility. However, if our current facility is damaged, suffers any form of

delay or regulatory challenges, we experience slowdowns or problems with the construction of our new facilities 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 and our third-party manufacturers may also encounter difficulties or delays in manufacturing of our product candidates or the plasmid used in the production of our product candidates. Geopolitical actions, natural disaster or a widespread health emergency, such as the recent outbreak of a novel strain of coronavirus named COVID-19 that initially emerged in China and has since spread globally, could impact our supply chain. To the extent that we or our third-party manufacturers are located in geographies affected by these matters, it may result in the temporary closing of manufacturing facilities and may increase the costs associated with manufacturing our product candidates.

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 have in the past, and may in the future, collaborate with third parties for the development, manufacture 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 have entered into collaboration agreements with third parties for the development and commercialization of our product candidates, including our Collaboration and License Agreement with Janssen for the development and

commercialization of AAV-CNGB3, AAV-CNGA3 and AAV-RPGR. We have also entered into a manufacturing research collaboration agreement with Janssen to further develop processes for manufacturing AAV viral vectors. We may seek additional collaborative relationships in the future. 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.

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, and the National Institute of Dental and Craniofacial Research, or NIDCR, a division of the National Institutes of Health. We are a party to agreements with UCLB for certain technology and AAV vector-related patents and with Brandeis for certain preclinical technology for the treatment of ALS. Further, we are party to an agreement with NIDCR for technology relating to the treatment of Sjogren's syndrome. 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 UCLB, we are obligated to pay an annual management fee, milestone payments for certain commercial sales thresholds, and royalties. If we fail to comply with our obligations to UCLB, Brandeis, NIDCR, 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 proceedings 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. 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 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 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 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 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 on 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. 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 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 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 essentially shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction in 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 United States. 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, 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 December 31, 2019, we had 157 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 Chief Financial 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.

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.

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;
- 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, cyber 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.

Operating as a public company may 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. If we are unable 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 and our systems and those of our contractors and consultants may be vulnerable to cybersecurity risks.

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, it could result in a material disruption of our product candidate development programs or manufacturing operations. 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. A significant interruption to our manufacturing operations could delay the completion of clinical trials and increase the costs of those trials. 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. Increased cybersecurity threats pose a risk to this information, in addition to our and our contractors' and consultants' systems and networks. Despite our security measures, our information

technology and infrastructure may be vulnerable to cyber-attacks by hackers or internal bad actors, or breached due to employee error, a technical vulnerability, malfeasance or other disruptions that could have a negative impact, including loss or destruction of data (including confidential information). Although, to our knowledge, we have not experienced any such material security breach to date, we may experience cybersecurity incidents such as malware infections, phishing attempts, thefts of personal, confidential or proprietary information and other attempts at compromising our information technology that are typical for a company of our size in our market. Any security 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, result in significant expenses in implementing future security measures and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and financial results, 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 UK's withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our shares.

Following a national referendum and enactment of legislation by the government of the UK, the UK formally withdrew from the EU on January 31, 2020 and entered into a transition period that is scheduled to end on December 31, 2020. During the transition period, the status quo is maintained and the UK and the EU will continue to negotiate their future customs and trading arrangements, and other aspects of their relationship.

During the transition period, there will continue to be significant political and economic uncertainty about the future trading relationship between the UK and the EU and whether such terms will differ materially from the terms before the withdrawal, as well as regarding the possibility that a so-called "no deal" separation will occur if negotiations are not completed by the end of the transition period. Lack of clarity about future UK laws and regulations as the UK 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; tax and customs laws, intellectual property rights; environmental, health, and safety laws and regulations; immigration laws; employment laws; and transport laws, could decrease foreign direct investment in the UK, increase costs, disrupt supply chains, depress economic activity, and restrict our access to capital. If the UK and the EU are unable to negotiate mutually acceptable terms, barrier-free access between the UK 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 have been and may continue to be especially subject to increased market volatility. In addition, changes to UK border and immigration

policy could occur as a result of the withdrawal, affecting our ability to recruit and retain employees from outside the UK. Any of these factors could have an adverse effect on our business, financial condition, results of operations, and prospects.

Further, the UK's withdrawal from the EU has resulted in the relocation of the EMA from the United Kingdom to the Netherlands. This relocation has caused, and may continue to cause, disruption in the administrative and medical scientific links between the EMA and 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 EU and/or the UK.

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

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.

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 your purchase 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 “Item 1A. Risk Factors” section and elsewhere in this Form 10-K.

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. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. 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 does not exceed your purchase price, you may not realize any return on your investment in us and may lose some or all of your investment.

Our executive officers, directors and principal shareholders, if they choose to act together, have the ability to control or significantly influence all matters submitted to shareholders for approval.

As of December 31, 2019, our executive officers, directors and shareholders who owned more than 5% of our outstanding ordinary shares and their respective affiliates, in the aggregate, hold ordinary shares representing approximately 60.9% of our outstanding ordinary shares.

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

A significant portion of our total outstanding shares are eligible to be sold into the market, 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.

Our outstanding ordinary shares may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act, or to the extent that such shares have already been registered under the Securities Act and are held by non-affiliates of ours. Moreover, certain holders of ordinary shares have rights, subject to specified conditions, to include their ordinary 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 have registered all ordinary shares that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. Upon issuance, these ordinary shares can be freely sold in the public market, subject to volume limitations applicable to affiliates and any applicable lock-up agreements.

In addition, certain of our employees, executive officers, directors and affiliated stockholders have entered, or may enter into, Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the employee, director, officer or affiliated shareholder when entering into the plan, without further direction from the employee, officer, director or affiliated shareholder. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers, directors and affiliated stockholders also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Any sales of securities by these shareholders could have a negative impact on the trading price of our ordinary shares.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting 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 ("JOBS Act"), and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of our IPO. 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 our periodic reports filed with the SEC;

- 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.

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 are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common shares held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100 million during the most recently completed fiscal year and our voting and non-voting common shares held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404, and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

We may choose to take advantage of some, but not all, of the available exemptions for emerging growth companies and smaller reporting companies. 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 shares price may be more volatile.

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

As a public company, and particularly if we no longer qualify as an emerging growth company and smaller reporting company in the future, we incur and will continue to 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 Global Select 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 need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are 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, we engage 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, or our independent registered public accounting firm if we no longer qualify as an emerging growth company, will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. 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. If we identify one or more material weaknesses or determine we have inadequate internal controls, 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 cease to 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 relies in part on the research and reports that industry or securities analysts publish about us or our business. We do not control these analysts. Furthermore, 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.

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

Certain of our directors and management 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.

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 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 jurisdiction's courts against us or our directors or officers 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 are also 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.

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.

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 Cayman Islands law, we may only make distributions by way of dividend out of profits, or out of our share premium account (provided that immediately following the date that the dividend is proposed to be paid we are able to pay our debts as they fall due in the ordinary course of business). 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 Form 10-K for the year ended December 31, 2019 for additional information.

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.

Our board of directors conducts 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, 2019, 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, 2019 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 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.

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 of our ordinary shares 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 of our ordinary shares should consult their tax advisors regarding the potential application of these rules to their investment 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 UK carryforward tax losses which we may not be able to realize or which may be restricted following the Reorganization Transactions 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, 2019, we had federal and state NOL carryforwards in the United States of $27.6 million and $27.5 million, respectively, cumulative carryforward tax losses in the United Kingdom of $107.3 million, and $22.8 million in the Netherlands, 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 carryforwards incurred prior to January 1, 2018 in the amount of approximately $6.8 million and $6.7 million will begin to expire in 2036. The UK carryforward tax losses will continue indefinitely, subject to relevant restrictions, under current UK legislation. Under the Tax Act, U.S. federal NOL carryforwards generated after December 31, 2017 are not subject to expiration but such NOLs may only offset 80% of taxable income. The Netherland's NOL's expire after nine years from the date of inception. As of December 31, 2019, we also had orphan drug and research and development credits in the U.S. in the amount of $2.4 million.

The NOL carryforwards and UK carryforward tax losses are subject to review and possible adjustment by the U.S., UK and state tax authorities. NOL carryforwards and UK 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. We have conducted a review of changes in the ownership interest of significant shareholders and determined that as of December 31, 2018, there were no limitations in the UK. However, for U.S. purposes, we have determined that a change of ownership occurred in November 2016. We are still in the process of determining the annual limitation on losses that occurred prior to November 2016. 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 and orphan drug credits. As such, the U.S. research and development and orphan drug credits may change and may be subject to review and adjustment by the tax authorities.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Our principal office is located at 450 East 29th Street, New York, New York 10016, USA, where we lease 22,721 square feet of office and laboratory space. We lease this office space under a lease that terminates on October 31, 2026.

We also own a long leasehold interest in the ground rights where our 29,000 square foot manufacturing facility is located, at 92 Britannia Walk, London, United Kingdom. The long leasehold interest expires in 2126, and there is no facility rent due.

Additionally, we lease an 11,306 square foot office facility located at 34-38 Provost Street, London, United Kingdom and 6,679 square feet of laboratory facilities at 15 Ebenezer Street, London, United Kingdom. The office space lease terminates on September 8, 2029 and the laboratory leases terminate on May 24, 2027.

ITEM 3. LEGAL PROCEEDINGS

We are not subject to any material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

On June 8, 2018, our ordinary shares began trading on the Nasdaq Global Market under the symbol "MGTX." Prior to that time, there was no public market for our stock.

Holders of Record

As of March 8, 2020, there were 53 holders of record. The actual number of shareholders of our ordinary shares is greater than this number of record holders and includes shareholders who are beneficial owners but whose ordinary shares are held in street name by brokers and other nominees. This number of holders of record also does not include shareholders whose ordinary shares may be held in trust by other entities.

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.

Recent Sales of Unregistered Securities

In lieu of cash payment of an accounts payable, on July 7, 2019, the Company issued 19,807 shares to a vendor in the amount of $421,500.

ITEM 6. SELECTED FINANCIAL DATA

Not applicable.

ITEM 7. 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 our financial statements and the related notes appearing in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many important factors, including those set forth in the section of this Form 10-K captioned "Item 1A. Risk Factors" and elsewhere in this Form 10-K, our actual results could differ materially from the results described in, or implied by, the forward-looking statements contained in the following discussion and analysis. For convenience of presentation some of the numbers have been rounded in the text below.

Overview

We are a vertically integrated, clinical stage gene therapy company with six programs in clinical development 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 ophthalmology, salivary gland and neurodegenerative disease programs, 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 an exempted company incorporated under the laws of the Cayman Islands in 2018, and prior to that, we commenced operations as MeiraGTx Limited, a private limited company incorporated under the laws of England and Wales 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 ("GAAP"). Since our formation, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facilities 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, developing our business plan, 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 amyotrophic lateral sclerosis ("ALS"). In October 2018, we acquired Vector Neurosciences, Inc., a Delaware corporation. In connection with that acquisition, we acquired its rights to the clinical stage gene therapy product candidate adeno-associated virus encoding glutamic acid decarboxylase ("AAV-GAD") gene therapy program which had completed a randomized, sham-controlled Phase 2 study for treatment of Parkinson's disease. In October 2019, we acquired Arthrogen, B.V., a Netherlands corporation. To date, we have financed our operations primarily with cash on hand and proceeds from the sales of our Series A ordinary shares, Convertible Preferred C Shares and ordinary shares. Through December 31, 2019, we received gross proceeds of approximately $358.7 million from sales of our ordinary shares, Series A ordinary shares and convertible preferred C shares and $100.0 million from the collaboration, option and license agreement with Janssen Pharmaceuticals, Inc. ("Janssen"), one of the Janssen Pharmaceuticals Companies of Johnson & Johnson (the "Collaboration and License Agreement"). As of December 31, 2019, we had cash and cash equivalents of $227.2 million.

We are a clinical stage company and have not generated any product revenues to date. We have six clinical programs and a pipeline of preclinical programs. Since inception, we have incurred significant operating losses. Our net

losses for the years ended December 31, 2019 and 2018 were $54.8 million and $82.9 million, respectively. As of December 31, 2019, we had an accumulated deficit of $203.0 million. We do not expect to generate revenue from sales of any products for several years, if at all. In March 2019, we received an upfront payment in the amount of $100.0 million from the Collaboration and License Agreement. Additionally, pursuant to the Collaboration and License Agreement, we are eligible to receive research and development funding and potential milestone payments and royalties.

Our total operating expenses were $71.6 million and $78.1 million for the years ended December 31, 2019 and 2018, respectively. While we expect our operating expenses to increase substantially in connection with our ongoing development activities related to our product candidates, we believe that these increases will be partially offset by the research funding in connection with the Collaboration and License Agreement. We anticipate that our expenses will increase due to costs associated with our clinical development program targeting achromatopsia due to mutations in the *CNGB3* or *CNGA3* gene, inherited retinal dystrophy caused by mutations in *RPE65*, and X-Linked retinitis pigmentosa, or XLRP. In addition, we expect to continue incurring increasing costs associated with our clinical activities for AAV-AQP1 for the treatment of radiation-induced xerostomia and xerostomia associated with Sjogren's syndrome. We are currently working with regulatory agencies to determine the path forward for clinical development of AAV-GAD. 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 operations, 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.

As a result of these anticipated expenditures, we will require additional capital, 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, we expect to continue incurring 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 cash and cash equivalents at December 31, 2019, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into 2022. 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 and scaling our manufacturing facilities and processes;
- the costs of operating as a public company;
- the extent to which we in-license or acquire rights to other products, product candidates 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.

Highlights and Recent Developments

Recent Clinical Development Highlights

AAV-AQP1 for the treatment of Grade 2/3 Radiation-Induced Xerostomia:

- We continue to activate clinical trial sites in our recently initiated Phase 1/2 AQUAx study, with patients now being enrolled at three of five expected study sites. Dosing in the first cohort was completed in the first quarter of 2020.
- The single center Phase 1 dose-finding study of AAV-AQP1 also continues to enroll patients at the National Institutes of Health (NIH). Enrollment in the fourth dose escalation cohort is now ongoing.
- We expect to report preliminary data from the AQUAx clinical trial in the second half of 2020.

Janssen-partnered investigational gene therapies for the treatment of inherited retinal diseases:

- In the first quarter of 2020, the EMA granted PRIME and ATMP designations to AAV-RPGR. PRIME designation was granted based on clinical data from the ongoing Phase 1/2 trial. To be awarded PRIME, a medicine must demonstrate potential to benefit patients with unmet medical needs based on early clinical data. We expect to engage with global regulatory authorities in 2020 with the goal of optimizing and accelerating the development of AAV-RPGR.

- We expect to report data from the ongoing clinical trial of AAV-RPGR in 2020.

- We continue to advance the ongoing phase 1/2 studies of AAV-CNGB3 and AAV-CNGA3 for the treatment of achromatopsia (ACHM) associated with mutations in the *CNGB3* and *CNGA3* genes.

AAV-GAD for the treatment of Parkinson's Disease:

- We anticipate that we will file an Investigational New Drug application (IND) in the second half of 2020.

AAV-RPE65 for the treatment of RPE65-Associated Retinal Dystrophy:

- In 2019, we presented data from a Phase 1/2 clinical trial which demonstrated that, in addition to meeting its primary endpoint of safety, AAV-RPE65 demonstrated statistically significant improvement across several assesments of visual function. We expect to meet with global regulatory authorities in 2020 to determine the regulatory pathway for AAV-RPE65.

Recent Corporate Development Highlights

Second Viral Vector Manufacturing Facility and Plasmid Production Facility

- We have completed feasibility studies for a second cGMP viral vector manufacturing facility and a cGMP plasmid production facility.

- We anticipate that our plasmid production facility will be operational by the end of 2020 and expect to initiate construction of our viral vector facility in mid-2020.

Expanding Clinical, Regulatory, Manufacturing, MSAT and Preclinical Development Teams

- We continue to substantially increase key personnel across functional areas to support our broad pipeline of optimized investigational gene therapies. As of December 31, 2019, we had 157 employees.

Components of Our Results of Operations

License Revenue

Our license revenue consisted of the amortization of the upfront payment we received in connection with the Collaboration and License Agreement.

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, legal, 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 have also incurred and expect to continue 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,		
	2019	2018	Change
Ophthamology programs	$ 14,013,426	$ 7,069,280	$ 6,944,146
Salivary gland programs	3,369,795	1,136,355	2,233,440
Neurodegenerative diseases programs	3,611,093	5,164,761	(1,553,668)
Manufacturing	12,770,950	5,224,272	7,546,678
Other research and development costs	31,257,629	18,752,823	12,504,806
Research Funding	(28,105,030)	(224,576)	(27,880,454)
Research and Development Tax Credit	(12,042,204)	(3,502,692)	(8,539,512)
Total research and development expenses	$ 24,875,659	$33,620,223	$ (8,744,564)

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. These increases in research and development costs may be partially offset by the research funding provided in connection with the Collaboration and License Agreement we entered into in January 2019.

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 (loss) 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 Limited, Arthrogen B.V. and MeiraGTx B.V. are measured using the foreign subsidiaries' local currency as the functional currency. MeiraGTx UK II Limited's 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.

Income Taxes

The 2018 income tax provision consisted of current tax expense of $0 and a deferred tax benefit of $474,391. The 2018 deferred tax benefit was recorded due to the required intraperiod tax allocation resulting from the loss from continuing operations and other comprehensive income. An intraperiod tax allocation was not required for 2019.

Critical Accounting Policies and Use of Estimates

Management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with the accounting principles generally accepted in the United States of America. The preparation of these consolidated financial statements requires us to make estimates and judgements that affect the reporting amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgements, including those related to license and collaboration revenue, warrant liabilities, share-based compensation and accrued expenses. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgements about the carrying value of assets and liabilities that are not readily apparent from our sources. Actual results may differ from these estimates under different assumptions.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing in this Form 10-K, 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

The accompanying consolidated financial statements include the accounts of Meira Holdings and its wholly owned subsidiaries:

MeiraGTx Limited, a limited company under the laws of England and Wales ("Meira Limited);
MeiraGTx, LLC, a Delaware corporation ("Meira LLC");
MeiraGTx UK II Limited, ("Meira UK II"), a limited company under the laws of England and Wales;
Arthrogen, B.V., a Netherlands corporation ("Arthrogen")
BRI-Alzan, Inc., a Delaware corporation ("BRI-Alzan");
MeiraGTx B.V., a Netherlands corporation ("Meira BV");
MeiraGTx Neurosciences, Inc. a Delaware corporation ("Meira Neuro");

and
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.

Collaboration Arrangements

We evaluate our collaborative arrangements pursuant to Accounting Standards Codification (“ASC”) 808, *Collaborative Arrangements* (“ASC 808”) and ASC 606, *Revenue from Contracts with Customers* (“ASC 606”). We consider the nature and contractual terms of collaborative arrangements and assess whether the arrangement involves a joint operating activity pursuant to which we are an active participant and are exposed to significant risks and rewards with respect to the arrangement. If we are an active participant and exposed to significant risks and rewards with respect to the arrangement, we account for the arrangement as a collaboration under ASC 808. To date, we have entered into two separate collaboration agreements, both of which are with Janssen, which were determined to be within the scope of ASC 808.

ASC 808 does not address recognition or measurement matters related to collaborative arrangements. Payments between participants pursuant to a collaborative arrangement that are within the scope of other authoritative accounting literature on income statement classification are accounted for using the relevant provisions of that literature. If the payments are not within the scope of other authoritative accounting literature, the income statement classification for the payments is based on an analogy to authoritative accounting literature or if there is no appropriate analogy, a reasonable, rational and consistently applied accounting policy election. Payments received from a collaboration partner to which this policy applies may include upfront payments in respect of a license of intellectual property, development and commercialization-based milestones, and royalties.

Revenue Recognition

Arrangements with collaborators may include licenses to intellectual property, research and development services, manufacturing services for clinical and commercial supply, and participation on joint steering committees. We evaluate the promised goods or services to determine which promises, or group of promises, represent performance obligations. In contemplation of whether a promised good or service meets the criteria required of a performance obligation, we consider the stage of development of the underlying intellectual property, the capabilities and expertise of the customer relative to the underlying intellectual property, and whether the promised goods or services are integral to or dependent on other promises in the contract. When accounting for an arrangement that contains multiple performance obligations, we must develop judgmental assumptions, which may include market conditions, reimbursement rates for personnel costs, development timelines and probabilities of regulatory success to determine the stand-alone selling price for each performance obligation identified in the contract.

When we conclude that a contract should be accounted for as a combined performance obligation and recognized over time, we must then determine the period over which revenue should be recognized and the method by which to measure revenue. We generally recognize revenue using a cost-based input method.

The Collaboration and License Agreement is accounted for under ASC 808, however, as ASC 808 does not address recognition or measurement matters such as determining the appropriate unit of accounting or when the recognition criteria are met, we account for the consideration received from Janssen in accordance with ASC 606. In accordance with ASC 606, we recognize revenue when the customer or collaborator obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps:

i. identify the contract(s) with a customer;

ii. identify the performance obligations in the contract;

iii. determine the transaction price;

iv. allocate the transaction price to the performance obligations within the contract; and

v. recognize revenue when (or as) the entity satisfies a performance obligation.

We only apply the five-step model to contracts when we determine that it is probable we will collect the consideration we are entitled to in exchange for the goods or services we transfers to the customer.

At contract inception, once the contract is determined to be by analogy within the scope of ASC 606, we assess the goods or services promised within the contract to determine whether each promised good or service is a performance obligation. The promised goods or services for our arrangements typically consist of a license to our intellectual property and research, development and manufacturing services. We may provide options to additional items in such arrangements, which are accounted for as separate contracts when the customer elects to exercise such options, unless the option provides a material right to the customer. Performance obligations are promises in a contract to transfer a distinct good or service to the customer that (i) the customer can benefit from on its own or together with other readily available resources, and (ii) is separately identifiable from other promises in the contract. Goods or services that are not individually distinct performance obligations are combined with other promised goods or services until such combined group of promises meet the requirements of a performance obligation.

We determine transaction prices based on the amount of consideration we expect to receive for transferring the promised goods or services in the contract. Consideration may be fixed, variable, or a combination of both. At contract inception for arrangements that include variable consideration, we estimate the probability and extent of consideration we expect to receive under the contract utilizing either the most likely amount method or expected amount method, whichever best estimates the amount expected to be received. We then consider any constraints on the variable consideration and include in the transaction price variable consideration to the extent it is deemed probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

We then allocate the transaction price to each performance obligation based on the relative standalone selling price and recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) control is transferred to the customer and the performance obligation is satisfied. For performance obligations which consist of licenses and other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

We record amounts as accounts receivable when the right to consideration is deemed unconditional. When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded as deferred revenue.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in our consolidated balance sheet. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue – related party, current. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue – related party.

Income Taxes

Since we have recurring losses and a valuation allowance against deferred tax assets, there was no tax expense (benefit) for the year ended December 31, 2019. For the year ended December 31, 2018, we recognized a tax benefit of $(474,391).

As of December 31, 2019, we had federal and state net operating loss ("NOL") carryforwards in the United States of approximately $27.5 million and $27.6 million, respectively, in the UK of approximately $107.3 million and in the Netherlands of approximately $22.8, which are available to reduce future taxable income. The U.S. federal and state NOL carryforwards incurred prior to January 1, 2018 in the amount of approximately $6.8 million and $6.7 million, respectively, will begin to expire in 2036. The U.S. NOL incurred after December 31, 2017 and the UK NOL will be indefinitely carried forward. The Netherlands NOL's expire after nine years from the date of inception. As of December 31, 2019, we also had orphan drug and research and development credits in the U.S. in the amount of $2.4 million, which will begin to expire 2036.

Leases

We account for leases in accordance with ASC 842. We determine if an arrangement is a lease at contract inception. A lease exists when a contract conveys the right to control the use of identified property, plant, or equipment for a period of time in exchange for consideration. The definition of a lease embodies two conditions: (1) there is an identified asset in the contract that is land or a depreciable asset (i.e., property, plant, and equipment), and (2) we have the right to control the use of the identified asset. We account for the lease and non-lease components as a single lease component.

From time to time we enter into direct financing lease arrangements that include a lessee obligation to purchase the leased asset at the end of the lease term, a bargain purchase option, or provides for minimum lease payments with a present value of 90% or more of the fair value of the leased asset at the date of lease inception.

Operating leases where we are the lessee are included in right-of-use ("ROU") assets and lease obligations are included on our consolidated balance sheets. The lease obligations are initially and subsequently measured at the present value of the unpaid lease payments at the lease commencement date and subsequent reporting periods.

Finance leases where we are the lessee are included in ROU assets and lease obligations on our consolidated balance sheets. The lease obligations are initially measured in the same manner as for operating leases and are subsequently measured at amortized cost using the effective interest method.

Key estimates and judgments include how we determined (1) the discount rate we use to discount the unpaid lease payments to present value, (2) lease term and (3) lease payments.

ASC 842 requires a lessee to discount its unpaid lease payments using the interest rate implicit in the lease or, if that rate cannot be readily determined, its incremental borrowing rate. As most of our leases where we are the lessee do not provide an implicit rate, we use our incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments. Our incremental borrowing rate for a lease is the rate of interest we would have to pay on a collateralized basis to borrow an amount equal to the lease payments under similar terms. We use the implicit rate when readily determinable.

The lease term for all of our leases includes the non-cancellable period of the lease plus any additional periods covered by either a lessee option to extend (or not to terminate) the lease that is reasonably certain to be exercised, or an option to extend (or not to terminate) the lease controlled by the lessor.

The ROU asset is initially measured at cost, which comprises the initial amount of the lease liability adjusted for lease payments made at or before the lease commencement date less any lease incentives received.

For operating leases, the ROU asset is subsequently measured throughout the lease term at the carrying amount of the lease liability, minus any accrued lease payments, less the unamortized balance of lease incentives received. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

For finance leases, the ROU asset is subsequently amortized using the straight-line method from the lease commencement date to the earlier of the end of its useful life or the end of the lease term unless the lease transfers ownership of the underlying asset to us, or we are reasonably certain to exercise an option to purchase the underlying asset. In those cases, the ROU asset is amortized over the useful life of the underlying asset. Amortization of the ROU asset is recognized and presented separately from interest expense on the lease liability.

We have elected not to recognize ROU assets and lease liabilities for all short-term leases that have a lease term of 12 months or less at lease commencement. We recognize the lease payments associated with our short-term leases as an expense on a straight-line basis over the lease term.

We adopted ASU 2016-02 using a modified retrospective transition approach as of the effective date as permitted by the amendments in ASU 2018-11, which provides an alternative modified retrospective transition method. As a result, we were not required to adjust our comparative period financial information for effects of the standard or make the new required lease disclosures for periods before the date of adoption (i.e. January 1, 2019). We have elected to adopt the package of transition practical expedients and, therefore, have not reassessed (1) whether existing or expired contracts contain a lease, (2) lease classification for existing or expired leases or (3) the accounting for initial direct costs that were previously capitalized. We did not elect the practical expedient to use hindsight for leases existing at the adoption date. Further, we do not expect the amendments in ASU 2018-01: *Land Easement Practical Expedient* to have an effect on us because we do not enter into land easement arrangements.

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. Research funding under collaboration agreements and refundable research and development credits / 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 of 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 were not traded on a public exchange prior to our IPO in June 2018. Therefore, 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 account 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 had accounted 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. On July 1, 2018, we early adopted ASU 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, which simplifies the accounting for share-based payments granted to nonemployees for goods and services. The adoption did not have a material effect on the consolidated financial statements.

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.

Results of Operations

The following table summarizes our results of operations for the years ended December 31, 2019 and 2018, respectively

	2019	2018	Change
License revenue - related party	$ 13,291,956	$ —	$ 13,291,956
Operating expenses:			
General and administrative	46,684,297	44,483,938	2,200,359
Research and development	24,875,659	33,620,223	(8,744,564)
Total operating expenses	71,559,956	78,104,161	(6,544,205)
Loss from operations	(58,268,000)	(78,104,161)	19,836,161
Other non-operating income (expense)			
Foreign currency gain (loss)	3,199,774	(3,824,383)	7,024,157
Change in fair value of warrant liability	—	(1,514,775)	1,514,775
Other income	—	83,075	(83,075)
Interest income	370,603	53,408	317,195
Interest expense	(48,612)	(33,429)	(15,183)
Loss before income taxes	(54,746,235)	(83,340,265)	28,594,030
Benefit for income taxes	—	474,391	(474,391)
Net loss	$(54,746,235)	$(82,865,874)	$28,119,639

License Revenue

License revenue in the amount of $13.3 million for the year ended December 31, 2019 represents amortization of the $100.0 million upfront payment received in connection with the Collaboration and License Agreement entered into in January 2019.

General and Administrative Expenses

General and administrative expenses were $46.7 million for the year ended December 31, 2019, compared to $44.5 million for the year ended December 31, 2018. The increase of $2.2 million was primarily due to increases of $1.9 million in legal fees, $1.2 million in rent, $1.4 million in insurance, $0.6 million in consulting fees, $0.6 million in travel expenses, $0.3 million in director fees and $0.5 million in other general and administrative expenses, which was partially offset by a decreases of $3.7 million in share-based compensation and $0.6 million in payroll.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2019 were $24.9 million, compared to $33.6 million for the year ended December 31, 2018. The decrease of $8.7 million was primarily due to research funding provided to us under the Janssen collaboration agreements in the amount of $27.9 million and an increase in the refundable research and development credit in the United Kingdom of $8.6 million. These were partially offset by increases in costs of $9.2 million for clinical trial costs related to our ophthalmology and salivary gland programs, $7.5 million related to the manufacturing of our clinical trial materials, $4.5 million due to the restructuring of certain licenses, $4.3 million in payroll related costs, $1.7 million in share-based compensation, and $0.7 million in rent.

Foreign Currency Gain (Loss)

Foreign currency gain was $3.2 million for the year ended December 31, 2019 compared to a loss of $3.8 million for the year ended December 31, 2018. The change of $7.0 million was primarily due to a strengthening of the pound sterling against the U.S. dollar in 2019.

Change in Fair Market Value of Warrant Liability

We recorded $1.5 million change in fair value of a warrant liability for the year ended December 31, 2018, due to the revaluation of warrants, which were issued to certain investors in September and November 2017, using the Black-Scholes valuation model at June 7, 2018, when the warrants were exercised.

Income Taxes

The 2018 income tax provision consisted of current tax expense of $0 and a deferred tax benefit of $474,391. The 2018 deferred tax benefit was recorded due to the required intraperiod tax allocation resulting from the loss from continuing operations and other comprehensive income. An intraperiod tax allocation was not required for 2019.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. For the year ended December 31, 2019, we generated $20.0 million of positive cash flows from operations, primarily from the $100 million upfront payment received in connection with the Collaboration and License Agreement. However, prior to the year ended December 31, 2019, we did not generate positive cash flows from operations and there are no assurances that we will generate positive cash flows in the future. Additionally, there are no assurances that we will be successful in obtaining an adequate level of financing for the development and commercialization of our product candidates. 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 products manufactured to support preclinical studies and clinical trials, expanding our intellectual property portfolio, and providing general and administrative support for our operations. In addition, we expect to expand our manufacturing and supply chain capabilities in the coming months. 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 do not currently have any approved products and have never generated any revenue from product sales. We have historically financed our operations primarily through cash on hand and proceeds from the sale of our ordinary shares, series A ordinary shares and convertible preferred C shares. In March 2019, we received $100.0 million in connection with the Collaboration and License Agreement, which also provides us with research funding, and we are eligible to receive potential milestone payments and royalties.

Cash Flows

We had $227.4 million and $68.2 million of cash and cash equivalents as of December 31, 2019 and 2018, respectively.

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

	For the years ended December 31,	
	2019	2018
Net cash provided by (used in) operating activities	$ 20,044,897	$ (58,887,870)
Net cash used in investing activities	(9,370,081)	(11,258,479)
Net cash provided by financing activities	148,234,904	130,040,415
Increase in cash	$158,909,720	$ 59,894,066

Operating Activities

During the year ended December 31, 2019, our cash provided by operating activities of $20.0 million was primarily due to our receipt of a $100.0 million upfront payment received from the Collaboration and License Agreement, which was partially offset by a net loss of $54.8 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 net loss included non-cash charges of $4.8 million, which consisted of $16.0 million of share-based compensation, $2.0 million for shares issued in connection with license agreements, depreciation of $2.2 million and lease obligations of $1.1 million, which was partially offset by a foreign currency gain of $3.2 million. Additionally, operating assets, consisting of accounts receivable, prepaid expenses, tax incentive receivable, security deposits and other current assets, increased by $35.5 million and operating liabilities, consisting of accounts payable, accrued expenses, and deferred revenue, increased by $92.2 million.

During the year ended December 31, 2018, our cash used in operating activities of $58.9 million was primarily due to our net loss of $82.9 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 $27.9 million, which consisted of $17.9 million of share-based compensation, issuance of shares for acquired research and development in the amount of $3.0 million, change in fair value of warrant liability in the amount of $1.5 million, depreciation of $2.1 million, and a foreign currency loss of $3.9 million, which was partially offset by an income tax benefit of $0.5 million. Additionally, current assets, consisting of prepaid expenses, other current assets and security deposits increased by $3.9 million. Current liabilities, consisting of accounts payable, accrued expenses, deferred rent, due to affiliate and other liabilities, decreased by $0.1 million

Investing Activities

Net cash used in investing activities for the years ended December 31, 2019 and 2018 of $9.4 million and $11.3 million, respectively, consisted primarily of purchases of property and equipment for our manufacturing, laboratory and process development facilities and buildout costs of our new facilities.

Financing Activities

Net cash provided by financing activities was $148.2 million for the year ended December 31, 2019, which consisted primarily of gross proceeds of $155.2 million from a private placement and a public offering of our ordinary shares, which was offset by $7.5 million in offering costs.

Net cash provided by financing activities was $130.0 million for the year ended December 31, 2018, represented proceeds of $65.6 million from the issuance of Ordinary Shares in connection with our initial public offering, $56.1 million from the issuance of Convertible Preferred C Shares and $9.7 million from the exercise of warrants, which was partially offset by the repayment of a note payable in the amount of $1.4 million.

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.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012, (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.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

We are exposed to market risks in the ordinary course of our business. These risks primarily include foreign currency exchange rate sensitivities and interest rate risk.

We currently operate in the United States and the United Kingdom. Our activities in these countries expose us to currency exchange rate fluctuations primarily between the U.S. Dollar and the British Pound Sterling and Euro. When the U.S. Dollar strengthens against these currencies, the U.S. Dollar value of non-U.S. Dollar based losses increases. To the extent that our international activities recorded in local currencies increase in the future, our exposure to fluctuations in currency exchange rates will correspondingly increase. With respect to our foreign currency exposures as of December 31, 2019, a 10% unfavorable movement in foreign currency exchange rates would not expose us to a significant increase in net loss. We have not engaged in derivative financial instruments as a means of hedging this financial statement risk.

We had cash and cash equivalents of $227.2 million as of December 31, 2019, which consist of non-interest-bearing and interest-bearing bank deposits. Other than accounts payable and accrued expenses incurred in the ordinary course of business, we had no other debt outstanding as of December 31, 2019. We had cash and cash equivalents of $68.1 million as of December 31, 2018, which consisted of non-interest-bearing and interest-bearing bank deposits. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant for us.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
FOR THE YEARS ENDED DECEMBER 31, 2019 AND 2018
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of MeiraGTx Holdings plc and Subsidiaries

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of MeiraGTx Holdings plc and Subsidiaries

(the Company) as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, shareholders' deficit and cash flows for each of the two years in the period ended December 31, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles.

Adoption of ASU No. 2016-02

As discussed in Note 2 to the consolidated financial statements, effective January 1, 2019, the Company changed its method of accounting for leases due to the adoption of Accounting Standards Update (ASU) No. 2016-02 Leases (Topic 842), and the related amendments. The Company adopted the new standards using the modified retrospective transition method.

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 11, 2020

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED BALANCE SHEETS

	December 31, 2019	December 31, 2018
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 227,233,384	$ 68,080,175
Accounts receivable - related party	23,337,377	—
Prepaid expenses	4,464,085	1,937,785
Tax incentive receivable	11,974,437	3,416,932
Other current assets	1,970,585	1,217,173
Total Current Assets	268,979,868	74,652,065
Property and equipment, net	23,858,108	22,014,237
Security deposits	951,138	105,085
In-process research and development	777,655	—
Restricted cash	123,376	123,376
Other assets	195,053	—
Right-of-use assets	29,002,448	—
TOTAL ASSETS	$ 323,887,646	$ 96,894,763
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 3,759,339	$ 3,042,861
Accrued expenses	18,083,757	11,991,697
Lease obligations, current	1,674,210	27,199
Deferred revenue - related party, current	25,678,515	—
Other current liabilities	—	437,053
Total Current Liabilities	49,195,821	15,498,810
Deferred revenue - related party	60,535,576	—
Lease obligations	21,504,340	7,097
Asset retirement obligations	1,654,755	128,119
Deferred rent	—	201,264
Deferred income tax liability	195,053	—
TOTAL LIABILITIES	133,085,545	15,835,290
COMMITMENTS		
SHAREHOLDERS' EQUITY:		
Ordinary Shares, $0.00003881 par value, 1,288,327,750 authorized 36,791,906 issued and outstanding at December 31, 2019 27,386,632 issued and outstanding at December 31, 2018	1,429	1,064
Capital in excess of par value	395,630,666	229,054,460
Accumulated other comprehensive (loss) income	(1,794,042)	293,666
Accumulated deficit	(203,035,952)	(148,289,717)
Total Shareholders' Equity	190,802,101	81,059,473
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	$ 323,887,646	$ 96,894,763

See Notes to Consolidated Financial Statements

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	For the Year Ended December 31, 2019	2018
License revenue - related party	$ 13,291,956	$ —
Operating expenses:		
General and administrative	$ 46,684,297	$ 44,483,938
Research and development	24,875,659	33,620,223
Total operating expenses	71,559,956	78,104,161
Loss from operations	(58,268,000)	(78,104,161)
Other non-operating income (expense):		
Foreign currency gain (loss)	3,199,774	(3,824,383)
Change in fair value of warrant liability	—	(1,514,775)
Other income	—	83,075
Interest income	370,603	53,408
Interest expense	(48,612)	(33,429)
Loss before income taxes	(54,746,235)	(83,340,265)
Benefit for income taxes	—	474,391
Net loss	(54,746,235)	(82,865,874)
Other comprehensive (loss) income:		
Foreign currency translation, net of tax of $0 and $474,391 in 2019 and 2018, respectively	(2,087,708)	2,316,143
Total comprehensive loss	$ (56,833,943)	$ (80,549,731)
Net loss	$ (54,746,235)	$ (82,865,874)
Accretion on convertible preferred C shares and warrants	—	(1,806,512)
Net loss attributable to ordinary shareholders	$ (54,746,235)	$ (84,672,386)
Basic and diluted adjusted net loss per ordinary share	$ (1.65)	$ (4.47)
Weighted-average number of ordinary shares outstanding	33,161,860	18,948,520

See Notes to Consolidated Financial Statements

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' EQUITY (DEFICIT)
FOR THE YEARS ENDED DECEMBER 31, 2019 AND 2018

	Convertible Preferred C Shares		Shareholders' Equity (Deficit)					
	Shares	Amount	Ordinary Shares	Amount	Capital in Excess of Par Value	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Equity (Deficit)
Balance at January 1, 2018	5,005,935	$ 51,338,631	8,826,190	$ 342	$ 20,080,713	$ (2,022,477)	$ (65,423,843)	$ (47,365,265)
Issuance of convertible preferred C shares in connection with payables	129,419	1,356,129	—	—	—	—	—	—
Issuance of convertible preferred C shares in connection with a license agreement	13,360	140,000	—	—	—	—	—	—
Sale of convertible preferred C shares, net of issuance costs of $690,475	5,425,124	56,159,119	—	—	—	—	—	—
Accretion of issuance costs on convertible preferred C shares	—	761,012	—	—	(761,012)	—	—	(761,012)
Accretion of warrants issued in connection with convertible preferred C shares	—	1,045,500	—	—	(1,045,500)	—	—	(1,045,500)
Exercise of warrants	927,594	9,720,000	—	—	4,194,408	—	—	4,194,408
Conversion of convertible preferred C shares into A ordinary shares	(11,501,432)	(120,520,391)	11,501,432	446	120,519,945	—	—	120,520,391
Sale of ordinary shares in initial public offering, net of issuance costs of $9,807,622	—	—	5,000,000	194	65,192,184	—	—	65,192,378
Issuance of ordinary shares in connection with Vector Neurosciences acquisition	—	—	202,500	9	2,990,241	—	—	2,990,250
Share-based compensation	—	—	1,856,510	73	17,883,481	—	—	17,883,554
Foreign currency translation, net of income taxes	—	—	—	—	—	2,316,143	—	2,316,143
Net loss for the year ended December 31, 2018	—	—	—	—	—	—	(82,865,874)	(82,865,874)
Balance at December 31, 2018	—	—	27,386,632	1,064	229,054,460	293,666	(148,289,717)	81,059,473
Issuance of ordinary shares in connection with a license agreement	—	—	158,832	6	1,966,334	—	—	1,966,340
Sale of ordinary shares in connection with public and private placements, net of issuance costs of $7,497,852	—	—	8,997,102	349	147,701,806	—	—	147,702,155
Issuance of ordinary shares in connection with payables	—	—	19,807	1	421,499	—	—	421,500
Exercise of share options	—	—	134,533	5	557,601	—	—	557,606
Share-based compensation	—	—	95,000	4	15,928,966	—	—	15,928,970
Foreign currency translation	—	—	—	—	—	(2,087,708)	—	(2,087,708)
Net loss for the year ended December 31, 2019	—	—	—	—	—	—	(54,746,235)	(54,746,235)
Balance at December 31, 2019	—	$ —	36,791,906	$ 1,429	$ 395,630,666	$ (1,794,042)	$ (203,035,952)	$ 190,802,101

See Notes to Consolidated Financial Statements

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS

	For the Year Ended December 31,	
	2019	2018
Cash flows from operating activities:		
Net loss	$ (54,746,235)	$ (82,865,874)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Ordinary shares issued in connection with license agreements	1,966,334	—
Preferred C shares issued in connection with license agreements	—	140,000
Share-based compensation expense	15,928,970	17,883,554
Foreign currency (gain) loss	(3,199,774)	3,824,383
Depreciation	2,238,560	2,053,220
Lease obligations	1,107,805	—
Deferred rent	—	(65,189)
Amortization of interest on asset retirement obligations	20,621	(38,301)
Change in fair value of warrant liability	—	1,514,775
Issuance of shares for acquired research and development expense	—	2,990,250
Benefit for income taxes	—	(474,391)
(Increase) decrease in operating assets:		
Accounts receivable - related party	(23,886,573)	—
Prepaid expenses	(2,259,984)	(35,465)
Tax incentive receivable	(8,401,283)	(3,502,692)
Other current assets	(178,805)	(181,773)
Security deposits	(796,753)	(115,573)
Increase (decrease) in operating liabilities:		
Accounts payable	(8,681)	(2,119,493)
Accrued expenses	6,518,766	2,529,568
Other current liabilities	—	436,161
Due to Kadmon	—	(861,030)
Deferred revenue - related party	85,741,929	—
Net cash provided by (used in) operating activities	20,044,897	(58,887,870)
Cash flows from investing activities:		
Purchase of property and equipment	(8,980,425)	(11,258,479)
Purchase of Arthrogen, net of acquired cash	(389,656)	—
Net cash used in investing activities	(9,370,081)	(11,258,479)
Cash flows from financing activities:		
Payments on lease obligations - financing leases	(24,857)	(30,852)
Exercise of warrants	—	9,720,000
Exercise of share options	557,606	—
Proceeds from the sale of ordinary shares	155,200,007	69,750,000
Issuance costs in connection with ordinary shares	(7,497,852)	(4,115,843)
Proceeds from the sale of convertible preferred C shares	—	56,849,594
Issuance costs in connection with convertible preferred C shares	—	(690,475)
Payment of note payable	—	(1,442,009)
Net cash provided by financing activities	148,234,904	130,040,415
Net increase in cash, cash equivalents and restricted cash	158,909,720	59,894,066
Effect of exchange rate changes on cash	243,489	(362,529)
Cash, cash equivalents and restricted cash at beginning of year	68,203,551	8,672,014
Cash, cash equivalents and restricted cash at end of year	$ 227,356,760	$ 68,203,551
Supplemental disclosure of non-cash transactions:		
Fixed asset acquisition included in accounts payable and accrued expenses at end of year	$ 1,519,454	$ 293,051
Lease obligations for right-of-use asset	$ 23,324,609	$ —
Reclassification of property and equipment to right-of-use asset	$ 7,409,789	$ —
Issuance of shares in connection with payables	$ 421,500	$ 1,356,129
Conversion of convertible preferred C shares into ordinary shares	$ —	$ 120,520,391
Reclassification of warrant liability upon exercise of warrants	$ —	$ 4,194,408
Issuance costs in connection with sale of ordinary shares in accounts payable and accrued expenses at end of year	$ —	$ 441,779
Asset retirement obligations in connection with a lease	$ 1,501,290	$ (29,804)
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 1,462	$ 34,546

See Notes to Consolidated Financial Statements

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Principal Business Activity

The Company

MeiraGTx Holdings plc and subsidiaries (the "Company" or "Meira Holdings"), an exempted company incorporated under the laws of the Cayman Islands, is a vertically integrated, clinical stage gene therapy company with six programs in clinical development and a broad pipeline of preclinical and research programs. The Company has 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, the Company has taken a portfolio approach by licensing, acquiring and developing technologies that give depth across both product candidates and indications. The Company's initial focus is on three distinct areas of unmet medical need: inherited retinal diseases, neurodegenerative diseases and severe forms of xerostomia. Though initially focusing on the eye, central nervous system and salivary gland, the Company intends to expand its focus in the future to develop additional gene therapy treatments for patients suffering from a range of serious diseases. The Company also owns and operates a current good manufacturing practices, or cGMP, multi-product, multi-viral vector manufacturing facility in London, United Kingdom ("UK"), which includes fill and finish capabilities and can supply the Company's clinical and potential commercial material.

Reorganization and Initial Public Offering

The Company commenced operations as MeiraGTx Limited, a private limited company incorporated under the laws of England and Wales in 2015. On June 7, 2018, in connection with its initial public offering (the "IPO"), the Company acquired all the issued and outstanding ordinary shares of MeiraGTx Limited pursuant to a series of reorganization transactions. The Company refers to these events in these notes as the "Reorganization Transactions." In the IPO, the Company sold 5,000,000 ordinary shares ("Ordinary Shares") at a public offering price of $15.00 per share, and received $65.2 million in net proceeds, after deducting underwriting discounts and commissions and offering expenses.

Acquisition

On October 17, 2019, the Company acquired 100% of the outstanding equity of Arthrogen B.V. ("Arthrogen"). Arthrogen is a biopharmaceutical company developing gene therapy for different indications, using viral mediated gene transfer. Arthrogen specializes in the development of viral gene therapy vectors, in particular adeno-associated virus (AAV-) based therapeutics. The acquisition of Arthrogen is part of the Company's continuing efforts to expand its focus to develop additional gene therapy treatments for patients suffering from a range of serious diseases. (See Note 3 for additional information).

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").

Liquidity

The Company 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, 2019 totaled $203,035,952, and management expects to incur

substantial 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. For the year ended December 31, 2019, the Company generated $20,044,897 of positive cash flows from operations. However, prior to the year ended December 31, 2019, the Company had not generated positive cash flows from operations. 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.

As of December 31, 2019, the Company had cash, cash equivalents and restricted cash in the amount of $227,356,760, which consisted of depository accounts. On January 30, 2019, the Company entered into a collaboration, option and license agreement with Janssen Pharmaceuticals, Inc. ("Janssen"), one of the Janssen Pharmaceuticals Companies of Johnson & Johnson (the "Collaboration Agreement"), for the research, development and commercialization of gene therapies for the treatment of inherited retinal diseases ("IRD"). Under the terms of the Collaboration Agreement, the Company received an upfront payment of $100,000,000. The Company will also receive funding for certain research, manufacturing, clinical development and commercialization costs, potential additional milestone payments upon the achievement of such milestones and royalties on future net sales of products. The Company estimates that its cash, cash equivalents and restricted cash on hand at December 31, 2019 will be sufficient to cover its expenses for at least the next twelve months from the date of issuance of these consolidated financial statements.

Risks and Uncertainties

The Company operates in an industry that is subject to intense competition, government regulation and rapid technological change. The Company's operations are subject to significant risk and uncertainties including financial, operational, technological, regulatory and other risks, including the potential risk of business failure.

The Company's capital resources and operations to date have been funded primarily with the proceeds from the Collaboration Agreement, private and public equity offerings and the IPO. In the future, the Company may seek to raise additional capital through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable it to complete the development and potential commercialization of its product candidates.

2. Summary of Significant Accounting Policies

Consolidation

The accompanying consolidated financial statements include the accounts of Meira Holdings and its wholly owned subsidiaries:

MeiraGTx Limited, a limited company under the laws of England and Wales ("Meira Limited");
MeiraGTx, LLC, a Delaware corporation ("Meira LLC");
MeiraGTx UK II Limited, ("Meira UK II"), a limited company under the laws of England and Wales;
Arthrogen, B.V., a Netherlands corporation ("Arthrogen");
BRI-Alzan, Inc., a Delaware corporation ("BRI-Alzan");
MeiraGTx B.V., a Netherlands corporation ("Meira BV");
MeiraGTx Neurosciences, Inc. a Delaware corporation ("Meira Neuro"); and
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.

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: collaboration revenue, the accounting for research and development costs, warrants, share-based compensation, leases and asset retirement obligations.

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 checking and money market accounts that are readily convertible into cash.

Financial Instruments

The carrying value of accounts receivable-related party, tax incentive receivable, other current assets, and accounts payable reported in the consolidated balance sheets equal or approximate fair value due to their short maturities.

Tax Incentive Receivable

Meira UK II is eligible to participate in a UK research and development tax incentive programs under which it is eligible to receive a cash refund from Her Majesty's Revenue & Customs ("HMRC") for a percentage of the qualified research and development costs expended by Meira UK II under the small and medium sized enterprises ("SME") program and the research and development expenditures credit ("RDEC") program. The SME cash refund is available to companies with less than 500 employee and annual aggregate revenue of less than 100.0 million euro or total aggregate assets less than 86.0 million euro during the reimbursable period. The Company's estimate of the amount of cash refund it expects to receive related to the SME and RDEC programs is included in tax incentive receivable in the accompanying consolidated balance sheets and such amounts are recorded as a reduction of research and development expense in the statements of operations. During the years ended December 31, 2019 and 2018, the Company recorded reductions to research and development expenses of $12.0 million and $3.5 million, respectively.

In addition, Meira UK II incurs Value Added Tax ("VAT") on services provided by UK vendors, which it is entitled to reclaim. The Company's estimate of the amount of cash refund it expects to receive related to VAT was $1.8 million and $1.1 million as of December 31, 2019 and 2018, respectively, which is included in other current assets in the accompanying consolidated balance sheet.

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 the Company's own credit risk.

The Company follows ASC Topic 820, *Fair Value Measurements and Disclosures*, or ASC 820, for application to financial assets and liabilities. In addition to defining fair value, the standard expands the disclosure requirements around fair value and establishes a fair value hierarchy for valuation inputs. The hierarchy prioritizes the inputs into three levels based on the extent to which inputs used in measuring fair value are observable in the market. Each fair value measurement is reported in one of the three levels which are determined by the lowest level input that is significant to the fair value measurement in its entirety. These levels are:

- Level 1: Observable inputs such as quoted prices in active markets for identical assets the reporting entity has the ability to access as of the measurement date;
- Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly; and
- Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The table below 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, 2019	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Restricted cash	$ 123,376	$ 123,376	$ —	$ —
Asset retirement obligations	$ 1,654,755	$ —	$ —	$ 1,654,755

		Fair Value Measurement Using:		
Description	December 31, 2018	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Restricted cash	$ 123,376	$ 123,376	$ —	$ —
Asset retirement obligations	$ 128,119	$ —	$ —	$ 128,119

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The table below represents a summary of the changes in fair value of the Company's Level 3 valuations from January 1, 2018 to December 31, 2019:

	Warrant Liabilities	Asset Retirement Obligations	Total
Balance as of January 1, 2018	$ 2,679,633	$ 178,419	$ 2,858,052
Change in fair value	1,514,775	(99,090)	1,415,685
Exercise of warrants	(4,194,408)	—	(4,194,408)
Additional asset retirement obligations during the period	—	69,286	69,286
Amortization of interest	—	(38,301)	(38,301)
Effects of exchange rate	—	17,805	17,805
Balance as of December 31, 2018	$ —	$ 128,119	$ 128,119
Additional asset retirement obligations during the period	—	1,270,262	1,270,262
Amortization of interest	—	20,621	20,621
Change in fair value	—	255,999	255,999
Effects of exchange rate	—	(20,247)	(20,247)
Balance as of December 31, 2019	$ —	$ 1,654,755	$ 1,654,755

The warrants were classified as liabilities because the underlying convertible preferred C shares ("Preferred Shares") had a redemption feature in the event of a change of control of the Company. On June 5, 2018, the warrants were exercised at which time the warrant liability was determined to be $4,194,408, which represented the difference in the market value of the Preferred Shares and the exercise price of the warrants. This resulted in an increase of the warrant liability in the amount of $1,514,775 for the period prior to exercise on June 5, 2018. The related warrant liability of $4,194,408 was reclassified as Capital in Excess of Par Value upon exercise.

The fair values of the warrants were estimated using the Black-Scholes valuation model with the following assumptions:

	June 4, 2018	December 31, 2017
Risk-free interest rate	1.77 %	1.72 %
Expected volatility	80 %	80 %
Expected dividend yield	0	0
Expected life	1 day	9 months

For the unobservable inputs for the warrants, the expected volatility was determined at each measurement date by taking an average of the volatility of other publicly-traded peer biotechnology companies. The expected life was determined at each measurement date based upon the Company's estimate of the time until the Company had a conversion event, which occurred on June 5, 2018.

The fair value of the Preferred Shares were based upon recent issuances of the Company's Preferred Shares on or about those dates.

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

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.

Concentrations of Credit Risk

The Company maintains its cash and cash equivalents primarily in depository and money market accounts within two large financial institutions in the United States and one large financial institution in the United Kingdom. Cash balances deposited at these major financial banking institutions exceed the insured limit. The Company has not experienced any losses on its bank deposits and believes these deposits do not expose the Company to any significant credit risk.

Property, Plant and Equipment, Net

Property, plant and equipment 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 as follows:

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 material impairment charges in 2019 or 2018.

Leases

The Company accounts for leases in accordance with ASC 842. The Company determines if an arrangement is a lease at contract inception. A lease exists when a contract conveys the right to control the use of identified property, plant, or equipment for a period of time in exchange for consideration. The definition of a lease embodies two conditions: (1) there is an identified asset in the contract that is land or a depreciable asset (i.e., property, plant, and equipment), and (2) the Company has the right to control the use of the identified asset. The Company accounts for the lease and non-lease components as a single lease component.

From time to time the Company enters into direct financing lease arrangements that include a lessee obligation to purchase the leased asset at the end of the lease term, a bargain purchase option, or provides for minimum lease payments with a present value of 90% or more of the fair value of the leased asset at the date of lease inception.

Operating leases where the Company is the lessee are included in right-of-use ("ROU") assets and lease obligations are included on the Company's consolidated balance sheets. The lease obligations are initially and subsequently measured at the present value of the unpaid lease payments at the lease commencement date and subsequent reporting periods.

Finance leases where the Company is the lessee are included in ROU assets and lease obligations on the Company's consolidated balance sheets. The lease obligations are initially measured in the same manner as for operating leases and are subsequently measured at amortized cost using the effective interest method.

Key estimates and judgments include how the Company determined (1) the discount rate used to discount the unpaid lease payments to present value, (2) lease term and (3) lease payments.

ASC 842 requires a lessee to discount its unpaid lease payments using the interest rate implicit in the lease or, if that rate cannot be readily determined, its incremental borrowing rate. As most of the Company's leases where it is the lessee do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments. The Company's incremental borrowing rate for a lease is the rate of interest it would have to pay on a collateralized basis to borrow an amount equal to the lease payments under similar terms. The Company uses the implicit rate when readily determinable.

The lease term for all of the Company's leases includes the non-cancellable period of the lease plus any additional periods covered by either a lessee option to extend (or not to terminate) the lease that is reasonably certain to be exercised, or an option to extend (or not to terminate) the lease controlled by the lessor.

The ROU asset is initially measured at cost, which comprises the initial amount of the lease liability adjusted for lease payments made at or before the lease commencement date less any lease incentives received.

For operating leases, the ROU asset is subsequently measured throughout the lease term at the carrying amount of the lease liability, minus any accrued lease payments, less the unamortized balance of lease incentives received. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

For finance leases, the ROU asset is subsequently amortized using the straight-line method from the lease commencement date to the earlier of the end of its useful life or the end of the lease term unless the lease transfers ownership of the underlying asset, or the Company is reasonably certain to exercise an option to purchase the underlying asset. In those cases, the ROU asset is amortized over the useful life of the underlying asset. Amortization of the ROU asset is recognized and presented separately from interest expense on the lease liability.

The Company has elected not to recognize ROU assets and lease liabilities for all short-term leases that have a lease term of 12 months or less at lease commencement. Lease payments associated with short-term leases are recognized as an expense on a straight-line basis over the lease term.

The Company adopted ASU 2016-02 using a modified retrospective transition approach as of the effective date as permitted by the amendments in ASU 2018-11, which provides an alternative modified retrospective transition method. As a result, the Company was not required to adjust its comparative period financial information for effects of the standard or make the new required lease disclosures for periods before the date of adoption (i.e. January 1, 2019). The Company has elected to adopt the package of transition practical expedients and, therefore, have not reassessed (1) whether existing or expired contracts contain a lease, (2) lease classification for existing or expired leases or (3) the accounting for initial direct costs that were previously capitalized. The Company did not elect the practical expedient to use hindsight for leases existing at the adoption date. Further, the Company does not expect the amendments in ASU 2018-01: *Land Easement Practical Expedient* to have an effect because the Company does not enter into land easement arrangements.

Asset Retirement Obligations

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, the Company estimates the fair value of its 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 of 8%. Asset retirement obligations currently reported on the Company's consolidated balance sheets 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.

Preferred Shares

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

The Company accounted for its Preferred Shares under the requirements of ASC 480, *Distinguishing Liabilities from Equity*, 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 was presented as temporary equity and was increased by periodic accretions so that the carrying amount would equal the redemption amount at the estimated date that the Preferred Shares would 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 was recorded as accretion over the estimated life of the Preferred Shares. The accretion was added to net loss to arrive at the net loss attributable to ordinary shareholders in the calculation of loss per ordinary share.

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 consolidated 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 the optionees 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 had been no public market for the Company's Ordinary Shares until the Company's IPO on June 7, 2018, the estimated fair value of the Ordinary Shares until that time had 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 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.

The fair value of Ordinary Shares after the Company's IPO was determined based upon the closing share price on the date of grant.

Since the Company's Ordinary Shares had not been traded on a public exchange prior to the Company's IPO and have only been traded on a public exchange for a short period of time since the Company's IPO, 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 the optionees 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 Securities and Exchange Commission's ("SEC") 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.

Restricted Shares

In connection with certain service agreements and research agreements, the Company has granted restricted Ordinary Shares as compensation. The Ordinary Shares are recognized in the consolidated 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.

Collaboration Arrangements

The Company evaluates its collaborative arrangements pursuant to ASC 808, *Collaborative Arrangements* ("ASC 808") and ASC 606, *Revenue from Contracts with Customers* ("ASC 606"). The Company considers the nature and contractual terms of collaborative arrangements and assesses whether the arrangement involves a joint operating activity pursuant to which the Company is an active participant and is exposed to significant risks and rewards with respect to the arrangement. If the Company is an active participant and is exposed to significant risks and rewards with respect to the arrangement, the Company accounts for the arrangement as a collaboration under ASC 808. To date, the Company has entered into two separate collaboration agreements, both of which are with Janssen, which were determined to be within the scope of ASC 808.

ASC 808 does not address recognition or measurement matters related to collaborative arrangements. Payments between participants pursuant to a collaborative arrangement that are within the scope of other authoritative accounting literature on income statement classification are accounted for using the relevant provisions of that literature. If the payments are not within the scope of other authoritative accounting literature, the income statement classification for the payments is based on an analogy to authoritative accounting literature or if there is no appropriate analogy, a reasonable, rational and consistently applied accounting policy election. Payments received from a collaboration partner to which this policy applies may include upfront payments in respect of a license of intellectual property, development and commercialization-based milestones, and royalties.

Refer to the discussion in Note 10 for further information related to the accounting for the Collaboration Agreement.

Revenue Recognition

Arrangements with collaborators may include licenses to intellectual property, research and development services, manufacturing services for clinical and commercial supply, and participation on joint steering committees. The Company evaluates the promised goods or services to determine which promises, or group of promises, represent performance obligations. In contemplation of whether a promised good or service meets the criteria required of a performance obligation, the Company considers the stage of development of the underlying intellectual property, the capabilities and expertise of the customer relative to the underlying intellectual property, and whether the promised goods or services are integral to or dependent on other promises in the contract. When accounting for an arrangement that contains multiple performance obligations, the Company must develop judgmental assumptions, which may include market conditions, reimbursement rates for personnel costs, development timelines and probabilities of regulatory success to determine the stand-alone selling price for each performance obligation identified in the contract.

When the Company concludes that a contract should be accounted for as a combined performance obligation and recognized over time, the Company must then determine the period over which revenue should be recognized and the method by which to measure revenue. The Company generally recognizes revenue using a cost-based input method.

The Collaboration Agreement with Janssen is accounted for under ASC 808, however, as ASC 808 does not address recognition or measurement matters such as determining the appropriate unit of accounting or when the recognition criteria are met, the Company accounts for the consideration received from Janssen in accordance with ASC 606. In accordance with ASC 606, the Company recognizes revenue when its customer or collaborator obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, it performs the following five steps:

i. identify the contract(s) with a customer;

ii. identify the performance obligations in the contract;

iii. determine the transaction price;

iv. allocate the transaction price to the performance obligations within the contract; and

v. recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it determines that it is probable it will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer.

At contract inception, once the contract is determined to be by analogy within the scope of ASC 606, the Company assesses the goods or services promised within the contract to determine whether each promised good or service is a performance obligation. The promised goods or services in the Company’s arrangements typically consist of a license to the Company’s intellectual property and research, development and manufacturing services. The Company may provide options to additional items in such arrangements, which are accounted for as separate contracts when the customer elects to exercise such options, unless the option provides a material right to the customer. Performance obligations are promises in a contract to transfer a distinct good or service to the customer that (i) the customer can benefit from on its own or together with other readily available resources, and (ii) is separately identifiable from other promises in the contract. Goods or services that are not individually distinct performance obligations are combined with other promised goods or services until such combined group of promises meet the requirements of a performance obligation.

The Company determines transaction price based on the amount of consideration the Company expects to receive for transferring the promised goods or services in the contract. Consideration may be fixed, variable, or a combination of both. At contract inception for arrangements that include variable consideration, the Company estimates the probability and extent of consideration it expects to receive under the contract utilizing either the most likely amount method or expected amount method, whichever best estimates the amount expected to be received. The Company then considers any constraints on the variable consideration and includes in the transaction price variable consideration to the extent it is deemed probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

The Company then allocates the transaction price to each performance obligation based on the relative standalone selling price and recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) control is transferred to the customer and the performance obligation is satisfied. For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company records amounts as accounts receivable when the right to consideration is deemed unconditional. When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded as deferred revenue.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in the Company’s consolidated balance sheet. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue – related party, current. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue – related party.

The Company’s collaboration revenue arrangements include the following:

Up-front License Fees: If a license is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from nonrefundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone Payments: At the inception of an agreement that includes research and development milestone payments, the Company evaluates each milestone to determine when and how much of the milestone to include in the transaction price. The Company first estimates the amount of the milestone payment that the Company could receive using either the expected value or the most likely amount approach. The Company primarily uses the most likely amount approach as that approach is generally most predictive for milestone payments with a binary outcome. Then, the Company considers whether any portion of that estimated amount is subject to the variable consideration constraint (that is, whether it is probable that a significant reversal of cumulative revenue would not occur upon resolution of the uncertainty.) The Company updates the estimate of variable consideration included in the transaction price at each reporting date which includes updating the assessment of the likely amount of consideration and the application of the constraint to reflect current facts and circumstances.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any revenue related to sales-based royalties or milestone payments based on the level of sales.

Research and Development Services: The Company is incurring research and development costs, with Janssen responsible for up to 100% of the costs, depending on the type of research and development services being performed. The Company records costs associated with the development activities as research and development expenses in the consolidated statement of operations and comprehensive loss consistent with ASC 730, *Research and Development*. The reimbursement of the research and development costs by Janssen is representative of the joint risk sharing nature of the arrangement. The Company considered the guidance in ASC 808 and recognizes the payments received from Janssen as a reduction to research and development expense when the related costs are incurred.

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 for the drug product for the clinical studies and preclinical activities; facilities; supplies; rent, insurance, certain legal fees, share-based compensation, depreciation, other costs associated with clinical and preclinical activities and regulatory operations and acquisition of in-process research and development write-offs. Research funding under collaboration agreements and refundable research and development credits / tax credits are recorded as an offset to these costs.

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

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 Meira UK II, Arthrogen and Meira B.V. are measured using the foreign subsidiaries' local currency as the functional currency. Meira UK II's 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.

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 10).

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, 2019 and 2018, 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, 2019, the Company had no unrecognized tax benefits or related interest and penalties accrued.

Net Loss per Ordinary Share

Basic net loss per Ordinary Share is computed by dividing net loss 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 Ordinary Share equivalents 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 periods presented, basic and diluted net loss per Ordinary Share are the same as any additional Ordinary Share equivalents would be anti-dilutive.

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, 2019	December 31, 2018
Restricted Ordinary Shares subject to forfeiture	217,726	653,174
Share options	3,645,360	3,262,365
	3,863,086	3,915,539

Other Comprehensive Income (Loss)

Other comprehensive income (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. The only component of other comprehensive income (loss) impacting the Company is foreign currency translation.

Segment Information

Management has concluded it has a single reporting segment for purposes of reporting financial condition and results of operations.

The Company’s license revenue, research funding and deferred revenue from its License and Collaboration Agreement are generated in the United Kingdom.

The following table summarizes non-current assets by geographical area:

	December 31, 2019	December 31, 2018
United States	$ 14,354,792	$ 454,568
United Kingdom	39,476,700	21,788,130
Netherlands	1,076,286	—
	$ 54,907,778	$ 22,242,698

Accounting Pronouncements Recently Adopted

In February 2016, the FASB issued ASU No. 2016-02, *Leases* ("ASC 842" or "ASU 2016-02"). The amended guidance requires lessees to recognize lease liabilities and ROU assets on the balance sheet for all leases with initial terms longer than 12 months and provides enhanced disclosures on key information of leasing arrangements. In July 2018, further amendments were issued to clarify how to apply certain aspects of the amended lease guidance and to address certain implementation issues. The amended guidance was effective for the Company commencing on January 1, 2019. The adoption of the amended guidance materially affected the Company's consolidated balance sheet and the primary impact was the recognition of minimum commitments at present value of the Company's noncancelable operating leases as lease liabilities and corresponding ROU assets. In July 2018, the FASB issued ASU No. 2018-10, which provided narrow amendments to ASU 2016-02 to clarify how to apply the rate implicit in the lease, impairment of the net investment in the lease, lessee reassessment of lease classification, variable payments that depend on an index or rate and certain transition adjustments. In July 2018, the FASB also issued ASU No. 2018-11, which provides targeted improvements to ASU 2016-02 to provide entities the transition option to not apply the standard in the comparative periods presented in the year of adoption. The Company adopted the new standards effective January 1, 2019 using the modified retrospective transition method using the package of practical expedients and a discount rate of 8%, and elected to not apply the standard in the comparative periods presented in the year of adoption. Upon implementation, the Company recorded a ROU asset of $10,836,319, which included a reclassification from property and equipment of a fully paid lease entered into in 2018 in the amount of $7,409,789, and a corresponding lease obligation of $3,716,336.

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. This update was effective for the Company as of January 1, 2019. The adoption of the provisions of ASU 2016-16 did not have a material impact on the current financial statements.

On July 1, 2018, the Company early adopted ASU 2018-07, *Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU No. 2018-07") which simplifies the accounting for share-based payments granted to nonemployees for goods and services. The ASU supersedes ASC 505-50 and expands the scope of ASC 718 to include *all* share-based payment arrangements related to the acquisition of goods and services from both nonemployees and employees. The adoption of ASU No. 2018-17 did not have a material effect on the consolidated financial statements.

In July 2019, the FASB issued ASU 2019-07, *Codification Updates to SEC Sections - Amendments to SEC Paragraphs Pursuant to SEC Final Rule Releases No. 33-10532, Disclosure Update and Simplification, and Nos. 33-10231 and 33-10442, Investment Company Reporting Modernization and Miscellaneous Updates (SEC Update)*. ASU 2019-07 clarifies or improves the disclosure and presentation requirements of a variety of codification topics by aligning them with the SEC's regulations, thereby eliminating redundancies and making the codification easier to apply. ASU 2019-07 became effective upon issuance and the adoption of ASU 2019-07, which is applied prospectively, did not have an impact on the Company's current financial statements.

Recent Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which adds a new Topic 326 to the Codification and removes the thresholds that companies apply to measure credit losses on financial instruments measured at amortized cost, such as loans, receivables, and held-to-maturity debt securities. Under current GAAP, companies generally recognize credit losses when it is probable that the loss has been incurred. The revised guidance will remove all recognition thresholds and will require companies to recognize an allowance for credit losses for the difference between the amortized cost basis of a financial instrument and the amount of amortized cost that the company expects to collect over the instrument's contractual life. ASU 2016-13 also amends the credit loss measurement guidance for available-for-sale debt securities and beneficial interests in securitized financial assets. The guidance is applicable for fiscal years beginning after December 15, 2019 and interim periods within those years, however, the FASB extended the effective date for smaller reporting companies to fiscal years beginning after December 15, 2022. The Company is currently evaluating the potential impact of the adoption of this standard on its related disclosures.

In August 2018, the FASB issued ASU 2018-13, *Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurements*, which changes the fair value measurement disclosure requirements of ASC 820. The goal of the ASU is to improve the effectiveness of ASC 820's disclosure requirements by providing users of the financial statements with better information about assets and liabilities measured at fair value in the financial statements and notes thereto. The guidance is applicable for fiscal years beginning after December 15, 2019 and interim periods within those years. The Company is currently evaluating the potential impact of the adoption of this standard on its related disclosures.

In August 2018, the FASB issued ASU No. 2018-15, *Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract.* ASU 2018-15 requires that certain implementation costs incurred in a cloud computing arrangement be deferred and recognized over the term of the arrangement. The new standard is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019, and early adoption is permitted. The Company is currently evaluating the potential impact of the adoption of this standard on its results of operations, financial position and cash flows and related disclosures.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606* ("ASU 2018-18"). The standard amends Accounting Standards Codification 808, Collaborative Agreements and Accounting Standards Codification 606, Revenue from Contracts with Customers, to clarify the interaction between collaborative arrangement participants that should be accounted for as revenue under ASC 606. In transactions when the collaborative arrangement participant is a customer in the context of a unit of account, revenue should be accounted for using the guidance in Topic 606. The amendments in ASU 2018-18 are effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. The Company is currently evaluating the new guidance included in ASU 2018-18, but does not expect it to have a material impact on its consolidated financial statements.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740) – Simplifying the Accounting for Income Taxes*. ASU 2019-12 simplifies the accounting for income taxes by removing exceptions within the general principles of Topic 740 regarding the calculation of deferred tax liabilities, the incremental approach for intraperiod tax allocation, and calculating income taxes in an interim period. In addition, the ASU adds clarifications to the accounting for franchise tax (or similar tax), which is partially based on income, evaluating tax basis of goodwill recognized from a business combination and reflecting the effect of any enacted changes in tax laws or rates in the annual effective tax rate computation in the interim period that includes the enactment date. The ASU is effective for fiscal year beginning after December 15, 2020, and will be applied either retrospectively or prospectively based upon the applicable amendments. Early adoption is permitted. The Company has elected to adopt this ASU as of January 1, 2020 on a prospective basis. The Company does not believe that this new guidance will have a material impact on its condolidate financial statements and related disclosures.

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3. Acquisitions

Arthrogen B.V.

On October 17, 2019, the Company acquired 100% of the outstanding equity of Arthrogen, a biopharmaceutical company developing gene therapy for different indications, using viral mediated gene transfer. Arthrogen specializes in the development of viral gene therapy vectors, in particular adeno-associated virus (AAV-) based therapeutics. The acquisition of Arthrogen is part of the Company's continuing efforts to expand its focus to develop additional gene therapy treatments for patients suffering from a range of serious diseases.

The purchase price consideration was €500,000, or approximately $558,335 and the Company utilized cash on hand. The Company incurred €94,692, or approximately $105,740 in acquisition related costs that were expensed immediately and recorded within general and administrative expenses within the Company's consolidated statement of operations and comprehensive loss.

At the time of acquisition, the net assets acquired were comprised of cash and working capital and were recorded at their respective acquisition date fair values. The excess purchase price over the net tangible assets was ascribed to in-process research and development. The acquisition was not significant to the Company's consolidated financial statements; therefore, pro forma results of the operations related to this business acquisition for the year ended December 31, 2019 have not been presented. The immaterial results of Arthrogen's operations since October 17, 2019 have been included in the Company's consolidated financial statements.

Vector Neurosciences

On October 5, 2018, the Company entered into an agreement to acquire Vector Neurosciences Inc. ("Vector") pursuant to an Agreement and Plan of Merger (the "Merger Agreement") by and among the Company, Vector, VN Acquisition, Inc., a wholly-owned subsidiary of the Company ("Merger Sub 1"), VN Acquisition 2, Inc., a wholly-owned subsidiary of the Company ("Merger Sub 2"), the Vector stockholders named therein and the Vector stockholder representative, pursuant to which Merger Sub 1 was merged with and into Vector, with Vector being the surviving corporation ("Merger 1") and, immediately following Merger 1, Vector was merged with and into Merger Sub 2, with Merger Sub 2 being the surviving corporation (together with Merger 1, the "Merger"). As a result of the Merger, Vector is a wholly-owned subsidiary of the Company. The merger consideration to Vector's stockholders consisted of 225,000 shares of the Company's Ordinary Shares as initial merger consideration, consisting of 202,500 shares which were issued at the closing of the Merger and an additional 22,500 shares to be issued 18 months following the closing, subject to any indemnification claims under the Merger Agreement (See Note 9).

In addition, pursuant to the terms of the Merger Agreement, the Company will issue to Vector's stockholders additional Ordinary Shares equal to a maximum value of $21,000,000 if specified regulatory milestones are met and will make royalty payments to Vector's stockholders in an amount equal to a percentage of the value of sales of certain products developed based on the Vector assets, which royalty payments are also payable in Ordinary Shares. The number of Ordinary Shares to be issued in connection with such milestones and royalties will be based on the three-day average closing price of the Company's Ordinary Shares immediately prior to the date of determination of the value of the payment.

The Company determined this transaction represented an asset acquisition as substantially all of the value was in the intellectual property as defined by ASC 805, *Business Combinations* ("ASC 805"). The asset acquisition of in-process research and development was recorded at a fair value of $2,990,250 as of October 5, 2018. The acquired in-process research and development was immediately charged to research and development expense in the consolidated 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, 2019, the contingent milestone payments in the

aggregate amount of $21,000,000, and royalty payments have not been resolved and therefore have not been recorded as liability.

4. Prepaid Expenses

Prepaid expenses at December 31, 2019 and 2018 consist of the following:

	December 31, 2019	December 31, 2018
Insurance	$ 1,758,915	$ 623,314
Clinical Trial Costs	1,609,166	373,723
Research and Development	239,161	352,658
Dues and License Fees	264,123	169,073
Rent	183,952	88,784
Other	408,768	330,233
	$ 4,464,085	$ 1,937,785

5. Property, Plant and Equipment, net

Property, plant and equipment, net at December 31, 2019 and 2018 consist of the following:

	December 31, 2019	December 31, 2018
Leasehold Improvements	$ 17,557,316	$ 11,652,055
Capitalized Leasehold Interest	—	7,150,611
Manufacturing Equipment	5,647,484	3,779,950
Laboratory Equipment	3,700,632	1,485,544
Computer and Office Equipment	1,066,984	334,525
Furniture & Fixtures	441,101	88,660
	28,413,517	24,491,345
Less: Accumulated depreciation	(4,555,409)	(2,477,108)
	$ 23,858,108	$ 22,014,237

On January 1, 2019, in accordance with ASU 842, the Company reclassified the capitalized leasehold interest as a ROU Asset.

In connection with six leases, the Company has determined that it has an asset retirement obligation in the aggregate amount of $3,736,404 at the end of certain of its leases. The Company discounted the asset retirement obligations using an 8% discount rate and recorded an asset retirement obligation in the aggregate amount of $1,643,794, which is included in leasehold improvements and is being depreciated over the term of the respective leases.

Capitalized leases in the amount of $95,880 are included in computer and office equipment at December 31, 2019 and 2018, with accumulated depreciation of $95,880 and $69,912 at December 31, 2019 and 2018, respectively.

Depreciation expense was $2,238,560 and $2,053,220 for the years ended December 31, 2019 and 2018 respectively.

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6. Accrued Expenses

Accrued expenses at December 31, 2019 and 2018 were comprised of the following:

	December 31, 2019	December 31, 2018
Compensation and Benefits	$ 6,850,335	$ 5,731,438
Clinical Trial Costs	7,788,077	4,013,094
Professional Fees	486,743	914,540
Consulting	1,247,989	821,009
Rent	283,876	122,770
Fixed Assets	1,108,362	—
Other	318,375	388,846
	$ 18,083,757	$ 11,991,697

7. Notes Payable

On October 26, 2017, in connection with an amendment and termination of a 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 11). The note bore interest at the rate of 5% per year 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 amount of $1,472,433 during the year ended December 31, 2018. The Company recorded interest expense in the consolidated statements of operations and comprehensive loss in connection with the note in the amount of $17,386 for the year ended December 31, 2018.

8. Share-Based Compensation

Equity Incentive Plans

The Company’s 2018 Incentive Award Plan and 2016 Equity Incentive Plan (collectively, the “Plans”), were adopted by the Company’s board of directors and shareholders. Under the Plans, the Company has granted share options to selected officers, employees and non-employee consultants. The Company’s board of directors or a committee thereof administers the Plans. Options granted under the Plans have a maximum contractual term of ten years. Options granted generally vest 25% on the first anniversary of the date of grant and the balance ratably over the next 36 months. Options granted to directors when they join the board generally vest in 36 equal monthly installments following the date of grant, and annual options granted to directors generally vest on the earlier of the first anniversary of the date of grant or the day before the Company’s annual meeting of shareholders. Upon the adoption of the 2018 Incentive Award Plan, the Company ceased issuing awards under the 2016 Equity Incentive Plan. Under the 2018 Incentive Award Plan the Company initially reserved up to 4,150,461 shares for issuance, of which, 1,877,611 shares remain available for future issuance as of December 31, 2019. The number of shares available for issuance under the 2018 Incentive Award Plan 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 the Company's board of directors. In January 2020, the number of shares available for issuance under the 2018 Incentive Award Plan increased by 1,470,421 shares. Also, in January 2020, the Company's board of directors authorized the issuance of 505,000 restricted stock units to certain executives and up to 1,117,000 options to all other employees and consultants, in each case, under the 2018 Incentive Award Plan.

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A summary of the Company's share option activity related to employees, non-employee members of the board of directors and non-employee consultants as of and for the years ended December 31, 2019 and 2018 is as follows:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (years)
Outstanding at December 31, 2017	938,637	$ 5.12	
Granted	2,326,285	8.63	
Exercised	—	—	
Expired	—	—	
Forfeited	(10,557)	(5.51)	
Outstanding at December 31, 2018	3,254,365	7.64	9.24
Granted	3,645,360	17.94	
Exercised	—	—	
Expired	3,254,365	—	
Forfeited	—	—	
Outstanding at December 31, 2019	10,154,090	$ 9.31	8.45
Options exercisable at December 31, 2019	1,437,281	$ 7.30	7.89
Aggregate intrinsic value of options outstanding as of December 31, 2019	$ 39,261,423		
Aggregate intrinsic value of options exercisable as of December 31, 2019	$ 18,278,490		

The total fair value of options vested during the years ended December 31, 2019 and 2018 was $6,098,621 and $1,387,607, respectively.

The grant date fair values of the share options granted were estimated using the Black-Scholes option valuation model with the following ranges of assumptions (see Note 2):

	2019	2018
Risk-free interest rate	1.76 - 2.55%	2.32% - 2.84%
Expected volatility	90%	90%
Expected dividend yield	0%	0%
Expected life (in years)	5.5 - 6.1	5.5 - 9.5

The weighted average grant date fair value of options granted during the years ended December 31, 2019 and 2018 was $13.79 and $6.53, respectively.

As of December 31, 2019, the total compensation expense relating to unvested options granted that had not yet been recognized was $16,398,970, which is expected to be realized over a period of 4.0 years. The Company will issue shares upon exercise of options from Ordinary Shares reserved under the Plans.

Restricted Ordinary Shares

In 2015, in connection with certain service and consulting agreements, certain employees and a consultant were awarded an aggregate of 867,935 restricted Ordinary Shares of the Company. Such shares were subject to forfeiture over a three-year service period. The shares granted to the consultant and employees were valued at $7.72 and $7.76 per share, respectively, and were included in research and development expenses in the consolidated statements of operations and comprehensive loss over the requisite service period. As of December 31, 2019, all such shares were no longer subject to forfeiture as the three-year service period has been completed.

On June 7, 2018, 1,306,348 restricted Ordinary Shares, which represented 5% of the fully-diluted outstanding shares of the Company as of such date, were issued to certain members of senior management in accordance with their employment agreements. One-third of such shares vested immediately, with the balance vesting quarterly over the next eight quarters beginning three months after the effectiveness of the Company's registration statement on Form S-1 filed with the SEC on June 7, 2018 (the "Registration Statement"). The shares were valued at $15.00 per share and the related share-based compensation expense, which is recognized over the requisite service period, is included in general and administrative expenses in the consolidated statements of operations and comprehensive loss. Additionally, under the terms of the employment agreements, the Company was required to pay the income taxes incurred by the grantees in connection with the grant of those restricted shares.

Total compensation expense in connection with the issuance of those restricted Ordinary Shares, in the amount of $15,982,670 and $20,141,876, of which $6,531,744 and $10,156,868 was share-based and $9,450,926 and $9,985,008 was paid in cash, was recorded as general and administrative expense during the years ended December 31, 2019 and 2018, respectively (See Note 12).

A summary of the restricted Ordinary Shares is as follows:

	Ordinary Shares	$ Value
Non-vested at December 31, 2017	105,913	$ 865,861
Issued during 2018	1,306,348	19,595,220
Vested during 2018	(759,087)	(10,663,471)
Non-vested at December 31, 2018	653,174	9,797,610
Vested during 2019	(435,448)	(6,531,720)
Non-vested at December 31, 2019	217,726	$ 3,265,890

Ordinary Shares

On March 1, 2018, a funding milestone was met under the employment agreements for certain members of senior management. Accordingly, the employees were issued an aggregate of 550,162 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 incurred by the grantees in connection with the grant of those shares. Total compensation expense in connection with the issuance of those Ordinary Shares, in the amount of $6,456,215, of which $3,096,104 was share-based, was recorded as general and administrative expense during the year ended December 31, 2018.

On October 31, 2019, the Company issued 95,000 shares to a consultant in the amount of $1,372,750.

During the years ended December 31, 2019 and 2018 the Company recognized total share-based compensation expense in the accompanying consolidated statements of operations and comprehensive loss as follows:

	2019	2018
Research and development	$ 5,059,046	$ 3,372,054
General and administrative	10,869,924	14,511,500
Total share based compensation	$ 15,928,970	$ 17,883,554

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, 2019 and 2018.

9. Ordinary Shares, Preferred Shares and Shareholders' Deficit

Ordinary Share Issuances

2019

Private Placement

On February 27, 2019, the Company issued 5,797,102 ordinary shares in a private placement for gross proceeds of $80 million, excluding offering costs of approximately $2.4 million. Johnson & Johnson Innovation – JJDC, Inc. ("JJDC"), the investment arm of Johnson and Johnson and owner of Janssen, purchased 2,898,550 of the ordinary shares issued on the same terms and conditions as the other investors in the offering.

In connection with the offering, the Company also entered into a registration rights agreement whereby, promptly following the date on which the Company becomes eligible to use a registration statement on Form S-3, but in no event later than July 31, 2019, the Company shall prepare and file a registration statement covering the resale of all of the Registrable Securities, as defined in the agreement. The Company filed the Form S-3 on July 2, 2019 and the Form S-3 was declared effective on July 16, 2019.

Public Offering

On August 7, 2019, the Company issued 3,200,000 ordinary shares in a public offering for gross proceeds of $75 million, excluding offering costs of approximately $5.1 million.

License Agreement

As discussed in Note 11, on March 21, 2019, the Company issued 158,832 ordinary shares in connection with a license agreement. In accordance with the license agreement, the cost basis of the shares was based on the closing share price on January 31, 2019.

Other Issuances

On July 7, 2019, the Company issued 19,807 shares to a vendor in the amount of $421,500.

On October 31, 2019, the Company issued 95,000 shares to a consultant in the amount of $1,372,750.

2018

As discussed in Note 13, on March 1, 2018, a funding milestone was met under the employment agreements for certain members of senior management. Accordingly, the employees were issued an aggregate of 550,162 fully vested Ordinary Shares.

In connection with the Company's initial public offering, on June 7, 2018, the Company issued 5,000,000 Ordinary Shares at an offering price of $15.00 per share for gross proceeds of $75,000,000, excluding offering costs of $9,807,622.

Also, as discussed in Note 13, on June 7, 2018, upon the effectiveness of the Company's Registration Statement, 1,306,348 restricted Ordinary Shares, which represented 5% of the fully-diluted outstanding shares of the Company as of such date, were issued to certain members of senior management in accordance with their employment

agreements. One-third of such shares vested immediately, with the balance vesting quarterly over the next eight quarters.

On October 5, 2018, in connection with an acquisition, the Company issued 202,500 Ordinary Shares with an additional 22,500 shares to be issued 18 months following the closing, subject to any indemnification claims under the merger agreement.

Preferred Shares

Issuances

2018

During the year ended December 31, 2018, the Company issued 5,425,124 Preferred Shares at an offering price of approximately $10.48 per share for gross proceeds of $56,849,611, excluding offering costs of $690,475.

Also, during the year ended December 31, 2018, the Company issued 129,419 Preferred Shares in lieu of payment of accounts payable in the aggregate amount $1,356,129 to certain vendors.

On March 15, 2018, the Company issued 13,360 Preferred Shares in connection with a license agreement.

On June 5, 2018, the Company issued 927,594 Preferred Shares in connection with the exercise of 3,600,000 warrants.

On June 7, 2018, upon effectiveness of the Company's Registration Statement on Form S-1, all of the 11,501,432 outstanding Preferred Shares were automatically converted into 11,501,432 Ordinary Shares. In connection with the conversion of the Preferred Shares, $664,718 of unaccredited financing costs were fully accreted.

10. Income Taxes

For the years ended December 31, 2019 and 2018, the Company recognized a tax benefit of $0 and $(474,391), respectively.

As of December 31, 2019, the Company had federal and state net operating loss ("NOL") carryforwards which are available to reduce future taxable income of:

	Federal	State
United States	$ 27,552,418	27,493,036
United Kingdom	$ 107,287,003	—
Netherlands	$ 22,808,090	—

The U.S. federal and state NOL carry forwards incurred prior to January 1, 2018 in the amount of approximately $6.8 million and $6.7 million, respectively, will begin to expire in 2036. The U.S. NOL incurred after December 31, 2017 and the UK NOL will be indefinitely carried forward. The Netherlands NOL's expire after nine years from the date incurred. Also, as of December 31, 2019, the Company had orphan drug and research and development credits in the U.S. in the amount of $2,391,137 which will begin to expire 2036. The NOL carry forwards are subject to review and possible adjustment by the U.S., UK, Netherlands 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, 2018, the Company had performed such an analysis and

determined that there were no limitations in the UK However, for U.S. purposes, the Company determined that a change of ownership occurred in November 2016. The Company is still in the process of determining the annual limitation on losses that occurred prior to November 2016. Subsequent ownership changes and proposed future changes to the UK (or U.S.) tax rules in respect of the utilization of losses carried forward may further affect the limitation in future years, if any. Additionally, the Company has begun a study on the completeness of the U.S. orphan drug and research and development credit.

The Company's pre tax earnings are as follows:

	December 31, 2019	December 31, 2018
United Kingdom	$ (37,993,537)	$ (73,359,978)
United States	(16,303,213)	(9,980,287)
Netherlands	(449,485)	—
	$ (54,746,235)	$ (83,340,265)

The Company is subject to the corporate tax rate in the UK as a limited UK corporation.

The following table summarizes a reconciliation of income tax benefit compared with the amounts at the UK statutory income tax rate:

	December 31, 2019		December 31, 2018	
Statutory rate	(10,401,785)	19.00 %	(15,834,650)	19.00 %
Permanent differences - other	(411,651)	0.75 %	1,438,934	(1.73)%
RTP and other adjustment	3,068,999	(5.61)%	387,509	(0.46)%
State and local rate, net of federal tax	(2,041,097)	3.73 %	(1,159,522)	1.39 %
U.K. Tax credit	1,278,072	(2.33)%	1,707,489	(2.05)%
U.S. Tax credit	(1,257,481)	2.30 %	(436,250)	0.52 %
Foreign tax rate differential	(347,301)	0.63 %	(171,693)	0.21 %
UK Rate change (17% at exxpected DTA turn)	362,092	(0.66)%	1,104,863	(1.33)%
US state rate change	—	0.00 %	(6,496)	0.01 %
Change in valuation allowance	9,750,153	(17.81)%	12,495,425	(14.99)%
Actual income tax benefit effective tax rate	—	0.00 %	(474,391)	0.57 %

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

	December 31, 2019	December 31, 2018
Current Tax Expense/(Benefit)		
United Kingdom	—	—
United States	—	—
Netherlands	—	—
Total Current	—	—
Deferred Tax Expense/(Benefit)		
United Kingdom	(3,036,499)	(8,888,096)
United States	(6,631,936)	(3,606,275)
Netherlands	(81,718)	—
Total Deferred	(9,750,154)	(12,494,371)
Change in Valuation Allowance	9,750,154	12,019,980
Total Income Tax Expense/(Benefit)	—	(474,391)

Income tax (benefit) expense for each year is allocated to continuing operations, discontinued operations, extraordinary items, other comprehensive income, the cumulative effects of accounting changes, and other charges

or credits recorded directly to shareholders' equity. ASC *740-20-45 Income Taxes, Intraperiod Tax Allocation, Other Presentation Matters* includes an exception to the general principle of intraperiod tax allocations. The codification source states that the tax effect of pretax income or loss from continuing operations generally should be determined by a computation that considers only the tax effects of items that are included in continuing operations. The exception to that incremental approach is that all items (i.e. other comprehensive income, discontinued operations, etc.) be considered in determining the amount of tax benefit that results from a loss from continuing operations and that benefit should be allocated to continuing operations. That is, when a company has a current period loss from continuing operations, management must consider income recorded in other categories in determining the tax benefit that is allocated to continuing operations. This includes situations in which a company has recorded a full valuation allowance at the beginning and end of the period, and the overall tax provision for the year is zero. The intraperiod tax allocation is performed once the overall tax provision has been computed and allocates that provision to various income statement (continuing operations, discontinued operations), other comprehensive income and balance sheet captions. While the intraperiod tax allocation does not change the overall tax provision, it results in a gross-up of the individual components. The level of application has been applied on the group level.

As the Company experienced a net loss from operations for the year ended December 31, 2018 and other comprehensive income from foreign currency translation adjustments, the Company allocated income tax expense against the components of other comprehensive income in 2018 using a 17% effective tax rate. Income tax benefit for the year ended December 31, 2018 includes a benefit $(474,391) due to the required intraperiod tax allocation. Conversely, other comprehensive income for the year ended December 31, 2018 includes income tax expense $474,391.

Deferred Tax Assets/(Liabilities)

	December 31, 2019			
	Total	UK	US	Netherlands
Deferred Tax Assets:				
Net operating loss carryforwards	$ 31,929,792	$ 18,238,791	$ 9,015,343	$ 4,675,658
Lease Liability	6,012,466	1,704,357	4,308,109	—
Other	2,581,842	485,724	2,108,121	(12,003)
R&D Credit	2,635,188	244,051	2,391,137	—
Deferred tax assets	43,159,288	20,672,923	17,822,710	4,663,655
Deferred Tax Liabilities:				
Indefinite-lived intangibles & Fixed Asset PPA	(173,431)	—	—	(173,431)
Right of use assets	(5,635,987)	(1,686,019)	(3,949,968)	—
Less: valuation allowance	(37,523,301)	(18,986,904)	(13,872,742)	(4,663,655)
Net deferred tax liability	$ (173,431)	$ —	$ —	$ (173,431)

	December 31, 2018			
	Total	UK	US	Netherlands
Deferred Tax Assets:				
Net operating loss carryforwards	$ 20,646,185	$ 15,997,008	$ 4,645,856	$ 3,321
Other	1,414,690	(46,604)	1,461,294	—
R&D Credit	1,133,656	—	1,133,656	—
Deferred tax assets	23,194,531	15,950,404	7,240,806	3,321
Less: valuation allowance	(23,194,531)	(15,950,404)	(7,240,806)	(3,321)
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, after consideration of the reversal of the deferred tax liabilities for the ROU assets and fixed assets, against its deferred tax assets at December 31, 2019 and 2018 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 UK 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 UK 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 UK 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 UK 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%.

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2019 and 2018, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations and comprehensive loss.

The Company files income tax returns in the United States, UK and Netherlands and various state jurisdictions. In the United States, tax years 2016, 2017 and 2018 remain subject to examination. In the United Kingdom, tax year 2018 remains subject to examination. In the Netherlands, tax years 2014, 2015, 2016, 2017 and 2018 remain subject to examination.

MeiraGTx Holdings plc is a UK tax resident with no earnings in its foreign subsidiaries and the Company does not expect any temporary basis difference in its investment in these subsidiaries to reverse in the foreseeable future. Therefore, the Company has not recorded deferred taxes on the outside basis difference in its foreign subsidiaries. It is not probable to compute the amounts, if any.

11. Related Party Transactions

Collaboration and License Agreements

Janssen Pharmaceuticals, Inc.

On January 30, 2019, the Company entered into a Collaboration Agreement with Janssen for the research, development and commercialization of gene therapies for the treatment of IRD. Under the agreement, Janssen paid the Company a non-refundable upfront fee of $100.0 million. Janssen and the Company will collaborate to develop the Company's current clinical programs in retinitis pigmentosa and two genetic forms of achromatopsia and Janssen has the exclusive right to commercialize these three product candidates ("Clinical IRD Product Candidates") globally.

Pursuant to the Collaboration Agreement, the Company and Janssen also agreed on a research collaboration to develop a pipeline of preclinical inherited retinal disease gene therapy candidates ("Research IRD Product Candidates"). The parties will select and prioritize the Research IRD Product Candidates and Janssen has the right to opt-in for a fee for each of the specified targets (each an "Option Target") to obtain certain development, manufacturing and commercialization rights for the Research IRD Product Candidates.

Unless terminated earlier under certain termination clauses, the Collaboration Agreement will continue in effect, on a product-by-product and country-by-country basis, until such time as the royalty terms expire in such country. The

Company has determined enforceable rights exist in the Collaboration Agreement as the termination clauses are substantive termination penalties by way of the non-refundable upfront fee and the reversion of any licensed intellectual property granted to Janssen upon the termination of the agreement.

On February 27, 2019, in connection with a private placement, the Company issued 2,898,550 ordinary shares to JJDC, the investment arm of Johnson and Johnson and owner of Janssen, on the same terms and conditions as the other investors in the offering. After the offering, JJDC became a related party.

Clinical IRD Product Candidates

Under the Collaboration Agreement, the Company and Janssen will jointly develop Clinical IRD Product Candidates to permit Janssen to commercialize such Clinical IRD Product Candidates under an exclusive license from the Company. In general, the Company will have the primary responsibility to develop each Clinical IRD Product Candidate in accordance with the development plan for each Clinical IRD Product Candidate, including where applicable, conducting any necessary research in order to submit the applicable regulatory filings to regulatory authorities. The Company will manufacture these products in its cGMP manufacturing facility for both clinical and commercial supply. Janssen will pay 100% of the clinical and commercialization costs of the products and the Company is eligible to receive untiered 20% royalties on net sales of products and additional development and commercialization milestones up to $340.0 million.

Research IRD Product Candidates

Under the Collaboration Agreement, the Company and Janssen will collaborate to develop Research IRD Product Candidates, with Janssen paying for the majority of the research costs. Janssen has the right to exclusively license any product coming out of the collaboration at the time of an investigational new drug application for an additional fee for each Research IRD Product Candidate. Janssen will then pay 100% of the clinical and commercialization costs for these Research IRD Product Candidates and the Company will receive an untiered royalty on net sales in the high teens as well as development milestones for each Research IRD Product Candidate.

Revenue Recognition under the Collaboration Agreement

The Collaboration Agreement is accounted for under ASC 808, however, ASC 808 does not address recognition or measurement matters. Therefore, the Company will account for the recognition and measurement of consideration under ASC 606. In determining the appropriate amount of revenue to be recognized under ASC 606, the Company performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company evaluated the potential performance obligations in the contract, which included the exclusive license to Clinical IRD Product Candidates, the research, development and manufacturing services (“the services”), and the participation in various joint committees and determined that none of the performance obligations by themselves were distinct. Goods and services that are not distinct are bundled with other goods or services in the contract until a bundle of goods or services that is distinct is created. The services, when combined with the licenses, represent a bundle and should be accounted for as a single performance obligation due to the relevance of the services to the value of the early-stage license and the potential for the intellectual property to be significantly modified during the services period. The Company also evaluated whether or not the right to purchase exclusive option rights for specified Research IRD Product Candidates represents future performance obligations and concluded that these represent a separate buyer decision at market rates, rather than a material right performance obligation. As such, these options have been excluded from the initial allocation of transaction price and the Company will account for these options as separate contracts when and if Janssen elects to exercise the options.

Under ASC 606, the Company recognized collaboration revenue using the cost-to-cost input method, which it believes best depicts the transfer of control to the customer. Under the cost-to-cost input method, the extent of progress towards completion is measured based on the ratio of actual costs incurred to the total estimated costs expected upon satisfying the combined performance obligation by the potential product candidate. Under this method, revenue is being recorded as a percentage of the estimated transaction price based on the extent of progress towards completion. Under ASC 606, the estimated transaction price includes variable consideration subject to constraints. The Company does not include variable consideration to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will occur when any uncertainty associated with the variable consideration is resolved. The estimate of the Company's measure of progress and estimate of variable consideration to be included in the transaction price will be updated at each reporting date as a change in estimate. The amount related to the unsatisfied portion will be recognized as that portion is satisfied over time.

Under ASC 606 the Company accounts for (i) the licenses it conveyed with respect to the Clinical IRD Product Candidates and (ii) its obligations to perform services as a single performance obligation under the Collaboration Agreement with Janssen on a product candidate basis. Janssen's right to purchase exclusive options to obtain certain development, manufacturing and commercialization rights are accounted for separately as they do not represent material rights, based on the criteria of ASC 606. Upon the exercise of any purchased option by Janssen, the contract promises associated with an Option Target would use a separate cost-to-cost model for purposes of revenue recognition under ASC 606.

During the year ended December 31, 2019, the Company received a $100.0 million non-refundable upfront fee from Janssen and allocated this amount plus other variable consideration not subject to constraint to each identified performance obligation using a combination of methods allowable under ASC 606. The Company applies the practical expedient in Topic 606 and does not include disclosures regarding amounts for variable consideration allocated to wholly-unsatisfied performance obligations or wholly-unsatisfied distinct goods that form part of a single performance obligation, if any. This variable consideration includes expected reimbursement of research and development costs. During the year ended December 31, 2019, the Company recognized $13,291,956, of the deferred revenue – related party as license revenue. The Company also recognized $27,296,062, during the year ended December 31, 2019 related to the reimbursement of research and development expenses, which was recorded as an offset to research and development expenses. As of December 31, 2019, the Company expects to recognize the remaining $86,214,091 in deferred revenue associated with the non-refundable upfront fee over the estimated research and development period using the cost-to-cost input method over an estimated period of approximately 5.5 years.

A summary of the deferred revenue recognition is as follows:

Non-refundable upfront fee from Janssen	$ 100,000,000
Deferred revenue recognized as license revenue during the year ended December 31, 2019	(13,291,956)
Effects of exchange rate	493,053
Deferred revenue at December 31, 2019	$ 86,214,091

Riboswitch Research Collaboration Agreement

On October 16, 2018, the Company entered into a riboswitch research collaboration agreement with Janssen, to develop regulatable gene therapy treatment using the Company's proprietary riboswitch technology. As part of the agreement, the Company will use its proprietary riboswitch technology to engineer regulatable gene therapy constructs encoding proprietary gene sequences from Janssen.

Upon execution of the agreement, Janssen paid the stage 1 fee in the amount of $658,667, and such payment was recorded as deferred revenue – related party. The stage 1 fee was being amortized over the estimated research term

of eight months. During the year ended December 31, 2019, the Company amortized the remaining $444,399 of the deferred revenue, which was recorded as an offset to research and development expenses. Additionally, the stage two fee, in the amount of $328,524 was recorded and fully amortized during the year ended December 31, 2019.

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. 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, 2019 and 2018 was approximately $306,000 and $636,000, respectively.

Future obligations under the agreement equal £165,878, or approximately $218,000 through, October 2020.

The amount due to UCL under the master services agreement at December 31, 2019 and 2018 is $166,404 and $389,101, respectively, and is included in accounts payable and accrued expenses on the Company's consolidated balance sheets.

License Agreement

Effective February 4, 2015, the Company entered into an exclusive worldwide license agreement with UCL Business, PLC ("UCL Business") to develop up to eight programs using certain ocular gene therapy technology. Under the terms of the agreement, the Company had agreed to pay UCL Business certain sales milestone payments, if achieved, in the aggregate amount of £39.8 million, or approximately $52.4 million using the exchange rate at December 31, 2019, and royalties on net sales, as defined upon commercialization. Additionally, the Company is responsible for all patent prosecution and maintenance costs incurred and has also agreed to pay UCL Business an annual maintenance fee of £50,000, or approximately $66,000, until the first commercial sale of a product. The agreement terminates 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.

On July 28, 2017, March 15, 2018 and September 7, 2018, the Company entered into additional exclusive worldwide license agreements with UCL Business under the same terms as the February 4, 2015 worldwide license agreement.

In January and February 2019, the Company amended and restated the following agreements: (i) the License Agreement, dated February 4, 2015, as amended, between the Company and UCL Business; (ii) the License Agreement, dated July 28, 2017, as amended, between the Company and UCL Business; and (iii) the License Agreement, dated March 15, 2018, between the Company and UCL Business to establish new stand-alone license agreements for the following inherited retinal disease programs: (a) achromatopsia ("ACHM") caused by mutations in CNGB3; (b) ACHM caused by mutations in CNGA3; (c) X-linked retinitis pigmentosa ("XLRP"); and (d) RPE65-mediated IRD.

The Company's obligation to pay UCL Business a share of certain sublicensing revenues, as was provided under the February 4, 2015 agreement, has been removed from each of the stand-alone agreements with respect to the IRD programs listed above. Each of the stand-alone agreements now reflects terms substantially similar to those of the February 4, 2015 agreement.

Additionally, under the new stand-alone agreement related to CNGB3 the Company paid UCL Business an upfront payment of £1,500,000, or approximately $1,976,000, and issued 158,832 of the Company's Ordinary Shares, which were valued at £1,500,000, or approximately $1,966,000.

The Company incurred research and development expenses under the agreements in the amount of $4,271,275, inclusive of the amendment payments of approximately $3,942,000, and $325,431 during the years ended December 31, 2019 and 2018, respectively.

Leases

ARE Lease

Effective July 1, 2016, the Company entered into a non-cancellable operating lease (the "ARE Lease") for laboratory and related office facilities in New York with ARE-East River Science Park, LLC ("ARE"), an entity that is under common control by an entity that is a minority shareholder of the Company and whose executive chairman and founder is a director of the Company. The ARE 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, 2018, the balance of deferred rent, representing the difference between cash rent paid and straight-line rent expense, was $201,264. As of December 31, 2019, and in accordance with ASC 842, the difference between cash rent paid and straight-line rent expense of $153,146 is reflected in the ROU asset.

Total rent expense under this operating lease was $487,555 for each of the years ended December 31, 2019 and 2018.

As of December 31, 2019, the aggregate future minimum rental payments under this lease are $1,128,269.

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 initially expired 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 in the amount of $123,676 at December 31, 2019 and 2018.

The restricted cash is included in long-term assets as of December 31, 2019 and 2018 and is measured using level 1 inputs.

The aggregate future minimum rental payments under this lease as of December 31, 2019 for years ending December 31 are as follows:

2020	$ 554,432
2021	573,837
Total future rent payments	$ 1,128,269

On January 28, 2020, the Company and ARE mutually agreed to terminate the lease with no further obligation for either party effective as of February 29, 2020.

Transition Services Agreement

Effective April 24, 2015, the Company entered into a transition services agreement (the "TSA") with Kadmon Holdings, Inc. ("Kadmon"), which owned 5.8% and 12.9% of the Company at December 31, 2019 and 2018, respectively, whereby Kadmon would provide office and laboratory facilities as well as certain other personnel support activities to the Company. Under the agreement, the Company was 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 terminated on April 24, 2018 and the Company is currently leasing office space on a month to month basis from Kadmon.

During the years ended December 31, 2019 and 2018, the Company incurred the following charges, which are included in loss from operations:

	2019	2018
Rent	$ 576,404	$ 557,698
Personnel	—	6,493
Other	—	6,334
Total charges incurred	$ 576,404	$ 570,525

During the year ended December 31, 2019 and 2018, the Company made cash payments to Kadmon totaling $576,404 and $1,431,555, respectively.

There were no cash payments due to Kadmon at December 31, 2019 and 2018.

12. Lease Obligations

The Company has commitments under operating leases for laboratory and office space. The Company also has finance leases for manufacturing space and office equipment. The Company's leases have initial lease terms ranging from 3 years to 108 years. Certain lease agreements contain provisions for future rent increases. Payments due under the lease contracts include fixed payments.

New York Sublease

Effective May 31, 2019, the Company entered into a non-cancelable operating sublease with an unrelated third party for laboratory and office space in New York. The lease, which expires on October 31, 2026, provides for monthly base rent and property management fees, including rent escalations and rent holidays, plus operating expenses during the lease term. The Company records monthly rent expense on a straight-line basis from June 20, 2019, the date the Company was allowed to access the leased premises, through October 31, 2026, when the sublease is set to terminate. In conjunction with this operating sublease, the Company recognized an initial operating lease ROU asset and corresponding operating lease liability of $11.8 million which is included in ROU assets and lease obligations on the consolidated balance sheets.

Total cash payments made under this operating lease were $180,000 for the year ended December 31, 2019.

Total rent expense recognized under this operating lease was $1,110,847, for the year ended December 31, 2019.

Tudor Street Lease

Effective June 11, 2019, the Company entered into a non-cancelable operating lease with an unrelated third party for warehouse space in London. The lease, which expires on June 10, 2029, provides for quarterly base rent and operating expenses during the lease term. The Company has the right to terminate this lease on June 10, 2024 by giving the landlord notice at least six months prior to such date. If the Company does not terminate the lease on June 10, 2024, then the annual rent is subject to a one-time adjustment based on the then current market conditions on June 11, 2024. As the Company does not expect to exercise its right to terminate the lease prior to the expiration date, the Company records monthly rent expense on a straight-line basis from June 11, 2019, the date the Company took possession of the leased premises, through June 10, 2029, when the lease is set to terminate. In conjunction

with this operating lease, the Company recognized an initial operating lease ROU asset and corresponding operating lease liability of £1.2 million, or approximately $1.5 million, which is included in ROU assets and lease obligations on the consolidated balance sheets.

Total cash payments made under this operating lease were £127,800, or approximately $168,000, for the year ended December 31, 2019.

Total rent expense recognized under this operating lease was £82,149, or approximately $108,000, for the year ended December 31, 2019.

Provost Street Lease

On May 29, 2019, the Company entered into an Agreement for Lease with an unrelated third party which provided a license to lease an entire building consisting of five floors of office and laboratory space in London. The leased premises were being renovated by the landlord with such renovations being completed in September 2019. Upon completion of the landlord renovations, the Company entered into a non-cancellable operating lease, which expires on September 8, 2029. The lease provides for quarterly base rent, including a rent holiday at the commencement of the lease, plus operating expenses during the lease term. The Company has the right to terminate this lease on September 8, 2024 by giving the landlord notice at least six months prior to such date. If the Company does not terminate the lease on by September 8, 2024, then the annual rent is subject to a one-time adjustment based on the then current market conditions on September 9, 2024. As the Company does not expect to exercise its right to terminate the lease prior to the expiration date, the Company records monthly rent expense on a straight-line basis from September 11, 2019, the date the Company took possession of the leased premises, through September 8, 2029, when the lease is set to terminate. In conjunction with this operating lease, the Company recognized an operating lease ROU asset and corresponding operating lease liability of £4.9 million, or approximately $6.5 million, which is included in ROU assets and lease obligations on the consolidated balance sheets.

Total cash payments made under this operating lease were £0, for the year ended December 31, 2019.

Total rent expense recognized under this operating lease was £238,222, or approximately $314,000, for the year ended December 31, 2019.

Ebenezer Street Leases

On July 27, 2018, two leases with an unrelated third party for office and laboratory facilities in London expired and the Company entered into two new non-cancellable operating leases with the same unrelated third party for the same office and laboratory facilities. The leases, which expire on May 24, 2027, provide for quarterly base rent, plus operating expenses, during the lease term. The Company has the right to terminate this lease on May 31, 2022 by giving the landlord notice at least six months prior to such date. If the Company does not terminate the lease on May 31, 2022, then the annual rent is subject to a one-time adjustment based on the then current market conditions. As the Company does not expect to exercise its right to terminate the lease prior to the expiration date, the Company records monthly rent expense on a straight-line basis from July 27, 2018 through May 24, 2027, when the leases are set to terminate. In conjunction with these operating leases, the Company recognized an initial operating lease ROU asset and corresponding operating lease liability of £1.7 million, or approximately $2.3 million, which is included in ROU assets and lease obligations on the consolidated balance sheets.

Total cash payments made under these operating leases were £274,969 and £137,485, or approximately $362,000 and $169,000, for the years ended December 31, 2019 and 2018, respectively.

Total rent expense recognized under these operating leases was £274,969 and £137,485, or approximately $362,000 and $169,000, for the years ended December 31, 2019 and 2018, respectively.

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

As of December 31, 2019, the Company has short term lease commitments amounting to approximately $52,000 on a monthly basis for three leases for office space that are month-to-month leases.

The components of lease cost for the year ended December 31, 2019 are as follows:

Finance lease cost		
Amortization of right-of-use assets	$	300,229
Interest on lease liabilities		2,409
Total Finance Lease Cost		302,638
Operating lease cost		2,384,048
Short-term lease cost		1,282,709
Total lease cost	$	3,969,395

Amounts reported in the consolidated balance sheets for leases where the Company is the lessee as of December 31, 2019 were as follows:

Operating leases	
Right of Use Asset	$ 21,857,600
Capitalized Lease Obligations	$ 23,127,813
Finance leases	
Right-of-Use Asset	$ 7,144,848
Capitalized Lease Obligations	$ 50,737
Weighted-Average Remaining Lease Term	
Operating leases	7.9 years
Finance leases	107.0 years
Weighted-Average Discount Rate	
Operating Leases	8.5 %
Finance Leases	7.3 %

Other information related to leases as of the year ended December 31, 2019 are as follows:

Cash paid for amounts included in the measurement of lease liabilities		
Operating cash flows from finance leases	$	28,187
Operating cash flows from operating leases	$	1,246,169
Financing cash flows from finance leases	$	2,355
Right-of-use assets obtained in exchange for lease liabilities		
Operating leases	$	23,279,980
Finance leases	$	44,629

Future minimum lease payments under non-cancellable leases as of December 31, 2019 are as follows:

	Operating Leases	Finance Leases
2020	$ 3,555,287	$ 26,451
2021	3,888,355	16,880
2022	3,955,076	12,660
2023	4,023,799	—
2024	3,826,294	—
Thereafter	10,708,509	—
Total undiscounted lease payments	$ 29,957,320	$ 55,991
Less: Imputed interest	(6,829,507)	(5,254)
Total lease liabilities	$ 23,127,813	$ 50,737

13. Commitments

Service Agreements

On April 27, 2015, the Company entered into service agreements with two senior officers of the Company. Under the terms of the agreements, the employees will receive aggregate compensation of £300,000, which has been increased to a maximum aggregate amount of £430,000 per year, or approximately $566,000. 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 after 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, 2019 and 2018, the Company recorded £944,500 and £1,001,000 or approximately $1,234,000 and $1,334,000, respectively, in research and development costs under these agreements. Future obligations to be paid under these agreements equal £157,000, or approximately $207,000 at December 31, 2019.

In connection with the service agreements, on April 24, 2015, the employees were awarded, under a share award agreement (the "Share Award Agreement"), an aggregate of 696,933 restricted Ordinary Shares and 193 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 $7.76 per share and, in accordance with ASC 718, were charged to operations as share-based compensation ratably over the forfeiture period. As of December 31, 2019, all such shares were no longer subject to forfeiture as the three-year service period had been completed.

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, which automatically renew for successive one-year terms, the employees will receive annual compensation in the aggregate amount of $710,000, which has been 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 shares. 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 aggregate amount of $850,000, were subject to compensation committee approval and meeting certain future funding conditions. On February 28, 2018, the funding conditions were met.

Bonuses granted to the senior officers, which included their guaranteed and discretionary bonuses, for the years ended December 31, 2019 and 2018, in the aggregate amount of $5,403,000 and $3,415,000 were paid in January of the subsequent years.

Additionally, the agreements provided for equity incentives of up to an aggregate 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. On June 7, 2018, an additional milestone was met. Accordingly, the employees were issued an aggregate of 5% of the fully-diluted outstanding shares of the Company as of such date (see Note 9).

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 $2,418,750, as of December 31, 2019.

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 170,809 restricted Ordinary Shares. Under the consulting agreement, such shares were 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 $7.72 per share and were charged to general and administrative expenses upon the expiration of each forfeiture period. For the years ended December 31, 2019 and 2018, the Company recorded $0 and $263,970, respectively, in general and administrative expense under this agreement. As of December 31, 2019, all such shares were no longer subject to forfeiture as the three-year service period had been completed.

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 years ended December 31, 2019 and 2018 were $117,592 and $111,938, respectively. Future obligations to be paid under the CRADA, as amended, through March 25, 2021 equal $106,250.

On March 22, 2016, the Company entered into another CRADA with the NIDCR and NIH for the treatment of *Sjögren's syndrome* associated salivary hypofunction. The CRADA provided 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 *Sjögren's syndrome* CRADA will be determined at a later date. Total research and development expenses under this agreement for the years ended December 31, 2019 and 2018 were $92,657 and $418,000, respectively. There are no future obligations to be paid under the agreement.

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 6,441 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. The Company further amended this agreement, effective October 18, 2018 to

include additional costs related to the research. Total research and development expenses under this agreement, as amended, for the years ended December 31, 2019 and 2018 were $1,756,487 and $1,625,152, respectively. Future obligations to be paid under the agreements are $206,984.

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, 2019 and 2018 were $20,613 and $143,073, respectively.

License Agreements

On September 7, 2018, the Company entered into an exclusive licensing agreement with the National Institutes of Health for worldwide rights to expanded indications for use of AAV-AQP1 for treatment of xerostomia (dry mouth) and xerophthalmia (dry eye) associated with *Sjögren's syndrome*. This agreement expands the Company's original exclusive licensing agreement with the NIH for exclusive worldwide rights to AAV-AQP1 that was executed as of November 9, 2017. AAV-AQP1 is currently in Phase 1/2 development for treatment of grade 2 or 3 radiation-induced xerostomia. Total research and development expenses under the agreement for the years ended December 31, 2019 and 2018 were $60,000 and $50,000, respectively.

Effective January 1, 2016, the Company acquired 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. Total research and development expenses under the agreement for the years ended December 31, 2019 and 2018 were $15,000 and $15,000, respectively.

14. Employee Benefit Plans

United States

On January 1, 2017, Meira LLC adopted a 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 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, Meira UK II adopted a defined contribution group personal pension plan that complies with HMRC for tax relief. All Meira UK II employees are eligible to participate in the plan upon joining the company and providing the required services. All eligible employees, if they elect to join the pension scheme, receive an employer pension contribution equal to 7.5% to 10.0% of their pensionable earnings. Currently, employees are not required to contribute, but may make optional contributions up to the annual allowance HMRC limits.

Under the HMRC requirements, current required 6+minimum employer contributions are 8-9%.

Netherlands

Arthrogen B.V. operates a defined contribution pension. All of its employees participate in the plan. All eligible employees receive an employer pension contribution and are also required to contribute.

During the years ended December 31, 2019 and 2018, employer contributions to all plans were $604,294 and $440,368, respectively.

15. Subsequent Events

Except for the item disclosed in Note 8, there have been no subsequent events through the date these financial statements were issued.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not Applicable.

ITEM 9A. CONTROLS AND PROCEDURES

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer (principal executive officer) and Chief Financial Officer (principal financial officer), evaluated, as of the end of the period covered by this Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")). Based on that evaluation, our Chief Executive Officer (principal executive officer) and Chief Financial Officer (principal financial officer) concluded that our disclosure controls and procedures were effective at the reasonable assurance level at the end of the period covered by this Form 10-K.

Management's Report on Internal Control Over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Exchange Act Rule 13a-15(f). Our internal control over financial reporting is a process designed under the supervision of our Chief Executive Officer and Chief Financial Officer, and affected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external reporting purposes in accordance with U.S. GAAP and includes policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets, (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of the effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies and procedures may deteriorate.

Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2019. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control—Integrated Framework (2013)*. Based on its assessment and those criteria, management has concluded that we maintained effective internal control over financial reporting as of December 31, 2019.

Exemption from Attestation Report of the Registered Public Accounting Firm on Internal Control Over Financial Reporting

This Form 10-K does not include an attestation report on our internal control over financial reporting from our independent registered public accounting firm since we qualify as an "emerging growth company" as defined under the JOBS Act.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item is incorporated by reference to our definitive proxy statement for our 2020 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2019.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item is incorporated by reference to our definitive proxy statement for our 2020 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2019.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Securities Authorized for Issuance Under Equity Compensation Plans (as of December 31, 2019)

The following table provides information as of December 31, 2019, regarding our ordinary shares that may be issued under the MeiraGTx Holdings plc 2016 Equity Incentive Plan, as amended (the "2016 Plan"), the MeiraGTx Holdings plc 2018 Incentive Award Plan (the "2018 Plan") and the MeiraGTx Holdings plc 2018 Employee Stock Purchase Plan (the "2018 ESPP").

Plan category:	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants, and Rights (a)	Weighted-Average Exercise Price of Outstanding Options, Warrants, and Rights (b)	Number of Securities Available for Future Issuance Under Equity Compensation Plans (excludes securities reflected in column(a)) (c)
Equity compensation plans approved by shareholders			
2016 Plan (1)	1,468,760	$ 5.45	—
2018 Plan (2)	2,176,600	$ 11.92	1,877,611
2018 ESPP (3)	—	—	783,032
Equity compensation plans not approved by shareholders	—	—	—
Total	3,645,360	$ 9.31	2,660,643

(1) In connection with our IPO, we assumed the 2016 Plan. As the 2016 Plan was previously approved by our shareholders and, as we will not make future grants or awards under these plans, it is listed as "approved by

shareholders." As such, the securities remaining available under the 2016 Plan have been excluded from the table above.

(2) Pursuant to the terms of the 2018 Plan, the number of ordinary shares available for issuance under the 2018 Plan automatically increases on each January 1, until and including January 1, 2028, by an amount equal to the lesser of: (a) 4% of the aggregate number of ordinary shares outstanding on the final day of the immediately preceding calendar year and (b) such smaller number of ordinary shares as is determined by our board of directors.

(3) Pursuant to the terms of the 2018 ESPP, the number of ordinary shares available for issuance under the 2018 ESPP automatically increases on each January 1, until and including January 1, 2028, by an amount equal to the lesser of: (a) 1% of the aggregate number of ordinary shares outstanding on the final day of the immediately preceding calendar year and (b) such smaller number of ordinary shares as is determined by our board of directors, subject to the limit set forth in the 2018 ESPP.

Other

The remaining information required by this Item is incorporated by reference to our definitive proxy statement for our 2020 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2019.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item is incorporated by reference to our definitive proxy statement for our 2020 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2019.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item is incorporated by reference to our definitive proxy statement for our 2020 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2019.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
2.1†	Agreement and Plan of Merger, dated October 5, 2018, by and among MeiraGTx Holdings plc, Vector Neurosciences Inc., VN Acquisition, Inc., VN Acquisition 2, Inc., the Vector stockholders named therein and the Vector stockholder representative, Stephen Kaplitt.	10-K	001-38520	2.1	3/26/19	
3.1	Amended and Restated Memorandum and Articles of Association of the Registrant.	10-Q	001-38520	3.1	8/7/19	
4.1	Specimen Share Certificate evidencing the ordinary shares of the Registrant.	S-1	333-224914	4.1	5/29/18	
4.2	Shareholder Agreement					*
4.3	Description of Securities					*
10.1#	2016 Equity Incentive Plan, as amended, and form of option agreements thereunder.	S-1/A	333-224914	10.1	5/29/18	
10.2#	2018 Incentive Award Plan and forms of award agreements thereunder.	S-1/A	333-224914	10.2	5/29/18	
10.3#	Non-Employee Director Compensation Program.					*
10.4#	Form of Indemnification Agreement for Directors and Officers.	S-1/A	333-224914	10.4	5/29/18	
10.5	License and Sub-Lease Agreement, dated May 31, 2019, between MeiraGTx LLC and Imclone Systems, LLC.	10-Q	001-38520	10.2	8/7/19	
10.6	Lease Agreement, effective February 2, 2016, among MeiraGTx Limited, Moorfields Eye Hospital NHS, Foundation Trust and Kadmon Corporation LLC.	S-1	333-224914	10.6	5/14/18	
10.7#	Employment Agreement, dated February 15, 2016, between MeiraGTx Limited and Alexandria Forbes, Ph.D., as amended.	S-1/A	333-224914	10.7	5/29/18	
10.8#	Employment Agreement, dated February 15, 2016 between MeiraGTx Limited and Richard Giroux, as amended.	S-1/A	333-224914	10.8	5/29/18	
10.9#	Employment Agreement, dated April 27, 2015, between MeiraGTx Limited and Stuart Naylor, Ph.D., as amended	S-1/A	333-224914	10.9	5/29/18	
10.10†	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.	S-1/A	333-224914	10.14	5/29/18	

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
10.11#	2018 Employee Share Purchase Plan.	S-1/A	333-224914	10.15	5/29/18	
10.12#	UK Sub-Plan Under the 2018 Incentive Award Plan.	10-K	001-38520	10.12	3/26/19	
10.13#	Form of Option Grant Notice and Option Agreement Under the UK Sub-Plan to the 2018 Incentive Award Plan.	10-K	001-38520	10.13	3/26/19	
10.14#	Employment Offer Letter, dated October 2, 2018, between MeiraGTx Holdings plc and Katherine Breedis	8-K	001-38520	10.1	10/9/18	
10.15	Lease agreement by and between Moorfields Eye Hospital NHS Foundation Trust and MeiraGTx UK II Limited, dated July 30, 2018	10-Q	001-38520	10.4	8/8/18	
10.16	Lease agreement by and between Moorfields Eye Hospital NHS Foundation Trust and MeiraGTx UK II Limited, dated July 30, 2018.	10-Q	001-38520	10.5	8/8/18	
10.17	Transfer of Title, dated December 14, 2018, and Lease, dated October 12, 2001, relating to the Pharmacy Manufacturing Unit, Britannia Walk, London, England	8-K	001-38520	10.1	12/14/18	
10.18	Overage Deed, dated December 14, 2018, between Moorfields Eye Hospital NHS Foundation Trust and MeiraGTx UK II Limited relating to the Pharmacy Manufacturing Unit, Britannia Walk, London, England	8-K	001-38520	10.2	12/14/18	
10.19†	Consulting Agreement, dated October 5, 2018, between MeiraGTx Holdings plc, Vector Consulting LLC, Michael G. Kaplitt, Matthew During, and Stephen B. Kaplitt.	10-K	001-38520	10.19	3/26/19	
10. 20†	License Agreement (RPE65), dated January 29, 2019, as amended and restated by and among UCL Business PLC, MeiraGTx UK II Limited and MeiraGTx Limited.	10-K	001-38520	10.20	3/26/19	
10. 21†	License Agreement (CNGB3), dated January 29, 2019, as amended and restated by and among UCL Business PLC, MeiraGTx Holdings plc, MeiraGTx UK II Limited and MeiraGTx Limited.	10-K	001-38520	10.21	3/26/19	
10. 22†	License Agreement (CNGA3), dated January 29, 2019, as amended and restated by and among UCL Business PLC, MeiraGTx UK II Limited and MeiraGTx Limited.	10-K	001-38520	10.22	3/26/19	

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
10. 23†	License Agreement (RPGR), dated February 5, 2019, as amended and restated by and among UCL Business PLC, MeiraGTx UK II Limited and MeiraGTx Limited.	10-K	001-38520	10.23	3/26/19	
10. 24†	Amendment No. 4 to Exclusive License Agreement, dated January 29, 2019, between UCLB and MeiraGTx Limited.	10-K	001-38520	10.24	3/26/19	
10. 25†	Collaboration, Option and License Agreement, dated January 30, 2019, by and among Janssen Pharmaceuticals, Inc., MeiraGTx UK II Limited and MeiraGTx Holdings plc.	10-K	001-38520	10.25	3/26/19	
10. 26†	Registration Rights Agreement, dated February 26, 2019, by and among MeiraGTx Holdings plc and the investors named therein.	8-K	001-38520	10.2	2/26/19	
10.27#	Employment Agreement, dated March 25, 2019, between MeiraGTx, LLC and Bruce Gottlieb.	10-Q	001-38520	10.1	5/14/19	
10.28#	Separation and Release Agreement, dated June 3, 2019, between MeiraGTx Holdings plc and Katherine Breedis.	8-K	001-38520	10.1	6/4/19	
10.29	Agreement for Lease with Landlord's Refurbishment Works, dated May 29, 2019, between MeiraGTx UK II Limited and Provost 1 Limited and Provost 2 Limited, including agreed form of Lease between MeiraGTx UK II Limited and Provost 1 Limited and Provost 2 Limited.	10-Q	001-38520	10.3	8/7/19	
10.30#	Form of Restricted Share Unit Grant Notice and Restricted Share Unit Agreement Under the 2018 Incentive Award Plan.					*
10.31#	Form of Restricted Share Unit Grant Notice and Restricted Share Unit Agreement Under the UK Sub-Plan to the 2018 Incentive Award Plan.					*
21	List of Subsidiaries					*
23.1	Consent of Ernst & Young LLP					*
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14(a)/15d-14(a) under the Securities Exchange Act of 1934, as amended.					*
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14(a)/15d-14(a) under the Securities Exchange Act of 1934, as amended.					*
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					**
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					**
101.INS	XBRL Instance Document.					*
101.SCH	XBRL Taxonomy Extension Schema Document.					*

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.					*
101.DEF	XBRL Taxonomy Definition Linkbase Document.					*
101.LAB	XBRL Taxonomy Label Linkbase Document.					*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.					*

* Filed herewith
** Furnished herewith
# Management contract or compensation plan or arrangement
† 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

Certain agreements filed as exhibits to this Form 10-K contain representations and warranties that the parties thereto made to each other. These representations and warranties have been made solely for the benefit of the other parties to such agreements and may have been qualified by certain information that has been disclosed to the other parties to such agreements and that may not be reflected in such agreements. In addition, these representations and warranties may be intended as a way of allocating risks among parties if the statements contained therein prove to be incorrect, rather than as actual statements of fact. Accordingly, there can be no reliance on any such representations and warranties as characterizations of the actual state of facts. Moreover, information concerning the subject matter of any such representations and warranties may have changed since the date of such agreements.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

MeiraGTx Holdings plc (Registrant)

Date: March 11, 2020

By: /s/ Alexandria Forbes
Alexandria Forbes
President and Chief Executive Officer and
Director (Principal Executive Officer)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Alexandria Forbes, Ph.D	President and Chief Executive Officer and Director (Principal Executive Officer)	March 11, 2020
Alexandria Forbes, Ph.D		
/s/ Richard Giroux	Chief Financial Officer (Principal Financial and Accounting Officer)	March 11, 2020
Richard Giroux		
/s/ Keith R. Harris, Ph.D.	Chairman of the Board and Director	March 11, 2020
Keith R. Harris, Ph.D.		
/s/ Martin Indyk	Director	March 11, 2020
Martin Indyk		
/s/ Ellen Hukkelhoven	Director	March 11, 2020
Ellen Hukkelhoven		
/s/ Nicole Seligman	Director	March 11, 2020
Nicole Seligman		
/s/ Arnold J. Levine, Ph.D.	Director	March 11, 2020
Arnold J. Levine, Ph.D.		
/s/ Joel S. Marcus	Director	March 11, 2020
Joel S. Marcus		
/s/ Neil Mendoza	Director	March 11, 2020
Neil Mendoza		
/s/ Thomas E. Shenk, Ph.D.	Director	March 11, 2020
Thomas E. Shenk, Ph.D.		

Exhibit 4.2

SHAREHOLDER AGREEMENT

OF

MEIRAGTX HOLDINGS PLC

DATED AS OF

7 JUNE 2018

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THIS SHAREHOLDER AGREEMENT is made on 7 June, 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 7 June 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.

SECTION 6. Additional Members; Preemptive Rights

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.

SECTION 7. Deposit and Use of Company Funds

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.

SECTION 8. Transfer of Shares

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 Exhibit B hereto (a "***Joinder Agreement***"), and shall thereby adhere and become a party to this Agreement.

SECTION 9. Warranties

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.

SECTION 10. Miscellaneous

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 7 June 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:	))))	/s/ Zandy Forbes	
		Signature	----------
		Name (block capitals)	ZANDY FORBES Director
Witness signature	/s/ Heather Leo ----------		
Witness name (block capitals)	HEATHER LEO		
Witness address	450 East 29th Street New York, NY 10016 ----------		

DESCRIPTION OF SECURITIES

The following summary of MeiraGTx Holdings plc's (the "Company") ordinary shares is based on and qualified by the Company's amended and restated memorandum and articles of association. In this "Description of Securities" discussion, we use the terms "we," "us" and "our" to refer to the Company.

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. On June 7, 2018, in connection with our initial public offering (the "IPO"), we acquired all the issued and outstanding ordinary shares of MeiraGTx Limited pursuant to a series of reorganization transactions, and, as a result, MeiraGTx Limited became a wholly owned subsidiary of the Company. We refer to these events as the "Reorganization Transactions." Prior to the Reorganization Transactions, MeiraGTx Holdings plc had not conducted any operations and had nominal assets and liabilities.

The principal legislation under which the Company operates and its shares are issued is the Cayman Islands Companies Law (2018 Revision) (the "Companies Law").

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

Share Capital

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 Company's amended and restated memorandum and 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.

Listing

Our ordinary shares are traded on the Nasdaq Global Select Market under the trading symbol "MGTX."

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.

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 Company 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 Company.

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 Company, making changes to our amended and restated memorandum and articles of association, or the voluntary winding up of the Company.

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, a

majority of whom (and, if a greater number of directors are present, a majority thereof) shall be present (either in person or otherwise provided in the amended and restated memorandum and articles of association) in the United Kingdom, and questions arising at any meeting shall be decided by a majority of votes.

Our amended and restated memorandum and articles of association 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.

Exhibit 10.3

MEIRAGTX HOLDINGS PLC

NON-EMPLOYEE DIRECTOR COMPENSATION PROGRAM

Non-employee members of the board of directors (the "***Board***") of MeiraGTx Holdings plc (the "***Company***") shall receive cash and equity compensation as set forth in this Non-Employee Director Compensation Program (this "***Program***"). The cash and equity compensation described in this Program shall be paid or be made, as applicable, automatically and without further action of the Board, to each member of the Board who is not an employee of the Company or any parent or subsidiary of the Company (each, a "***Non-Employee Director***") who is entitled to receive such cash or equity compensation, unless such Non-Employee Director declines the receipt of such cash or equity compensation by written notice to the Company. This Program shall remain in effect until it is revised or rescinded by further action of the Board. This Program may be amended, modified or terminated by the Board at any time in its sole discretion. The terms and conditions of this Program shall supersede any prior cash and/or equity compensation arrangements for service as a member of the Board between the Company and any of its Non-Employee Directors.

I. CASH COMPENSATION

A. Annual Retainers. Each Non-Employee Director shall receive an annual retainer of $25,000 for service on the Board.

B. Additional Annual Retainers. In addition, each Non-Employee Director shall receive the following annual retainers:

1. *Chairman of the Board or Lead Independent Director*. A Non-Employee Director serving as Chairman of the Board or Lead Independent Director shall receive an additional annual retainer of $25,000 for such service.

2. *Audit Committee*. A Non-Employee Director serving as Chairperson of the Audit Committee shall receive an additional annual retainer of $15,000 for such service. A Non-Employee Director serving as a member other than the Chairperson of the Audit Committee shall receive an additional annual retainer of $5,000 for such service.

3. *Compensation Committee*. A Non-Employee Director serving as Chairperson of the Compensation Committee shall receive an additional annual retainer of $10,000 for such service. A Non-Employee Director serving as a member other than the Chairperson of the Compensation Committee shall receive an additional annual retainer of $5,000 for such service.

4. *Nominating and Corporate Governance Committee*. A Non-Employee Director serving as Chairperson of the Nominating and Corporate Governance Committee shall receive an additional annual retainer of $10,000 for such service. A Non-Employee Director serving as a member other than the Chairperson of the Nominating and Corporate Governance Committee shall receive an additional annual retainer of $5,000 for such service.

5. *Science and Technology Committee*. A Non-Employee Director serving as Chairperson of the Science and Technology Committee shall receive an additional annual retainer of $10,000 for such service. A Non-Employee Director serving as a member other than the Chairperson of the Science and Technology Committee shall receive an additional annual retainer of $5,000 for such service.

C. Payment of Retainers. The annual retainers described in Sections I(A) and I(B) shall be earned on a quarterly basis based on a calendar quarter and shall be paid in cash by the Company in arrears not later than the fifteenth day following the end of each calendar quarter. In the event a Non-Employee Director does not serve as a Non-Employee Director, or in the applicable positions described in Section I(B), for an entire calendar quarter, the retainer paid to such Non-Employee Director shall be prorated for the portion of such calendar quarter actually served as a Non-Employee Director, or in such position, as applicable.

II. EQUITY COMPENSATION

Non-Employee Directors shall be granted the equity awards described below. The awards described below shall be granted under and shall be subject to the terms and provisions of the Company's 2018 Incentive Award Plan or any other applicable Company equity incentive plan then-maintained by the Company (the "***Equity Plan***") and shall be granted subject to award agreements, including attached exhibits, in substantially the form approved by the Board. All applicable terms of the Equity Plan apply to this Program as if fully set forth herein, and all grants of options hereby are subject in all respects to the terms of the Equity Plan and the applicable award agreement.

A. Initial Awards. Each Non-Employee Director who is initially elected or appointed to the Board shall receive an option to purchase 50,000 ordinary shares of the Company on the date of such initial election or appointment. The awards described in this Section II(A) shall be referred to as "***Initial Awards***." No Non-Employee Director shall be granted more than one Initial Award.

B. Subsequent Awards. A Non-Employee Director who (i) has been serving as a Non-Employee Director on the Board for at least six months as of the date of any annual meeting of the Company's shareholders and (ii) will continue to serve as a Non-Employee Director immediately following such meeting, shall be automatically granted an option to purchase 25,000 ordinary shares of the Company on the date of such annual meeting. The awards described in this Section II(B) shall be referred to as "***Subsequent Awards***." For the avoidance of doubt, a Non-Employee Director elected for the first time to the Board at an annual meeting of the Company's shareholders shall only receive an Initial Award in connection with such election, and shall not receive any Subsequent Award on the date of such meeting as well.

C. Termination of Employment of Employee Directors. Members of the Board who are employees of the Company or any parent or subsidiary of the Company who subsequently terminate their employment with the Company and any parent or subsidiary of the Company and remain on the Board will not receive an Initial Award pursuant to Section II(A) above, but to the extent that they are otherwise entitled, will receive, after termination from employment with the

Company and any parent or subsidiary of the Company, Subsequent Awards as described in Section II(B) above.

D. Terms of Awards Granted to Non-Employee Directors

1. *Exercise Price*. The per share exercise price of each option granted to a Non-Employee Director shall equal the Fair Market Value (as defined in the Equity Plan) of an ordinary share on the date the option is granted.

2. *Vesting*. Each Initial Award shall vest and become exercisable in thirty-six (36) substantially equal monthly installments following the date of grant, such that the Initial Award shall be fully vested on the third anniversary of the date of grant, subject to the Non-Employee Director continuing in service as a Non-Employee Director through each such vesting date. Each Subsequent Award shall vest and become exercisable on the earlier of the first anniversary of the date of grant or the day immediately prior to the date of the next annual meeting of the Company's shareholders occurring after the date of grant, in either case subject to the Non-Employee Director continuing in service on the Board as a Non-Employee Director through each such vesting date. Unless the Board otherwise determines, any portion of an Initial Award or Subsequent Award which is unvested or unexercisable at the time of a Non-Employee Director's termination of service on the Board as a Non-Employee Director shall be immediately forfeited upon such termination of service and shall not thereafter become vested and exercisable. All of a Non-Employee Director's Initial Awards and Subsequent Awards shall vest in full immediately prior to the occurrence of a Change in Control (as defined in the Equity Plan), to the extent outstanding at such time.

3. *Term*. The maximum term of each option granted to a Non-Employee Director hereunder shall be ten (10) years from the date the option is granted.

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MEIRAGTX HOLDINGS PLC
2018 INCENTIVE AWARD PLAN

RESTRICTED SHARE UNIT GRANT NOTICE

Capitalized terms not specifically defined in this Restricted Share Unit Grant Notice (the "***Grant Notice***") have the meanings given to them in the 2018 Incentive Award Plan (as amended from time to time, the "***Plan***") of MeiraGTx Holdings plc (the "***Company***").

The Company has granted to the participant listed below ("***Participant***") the Restricted Share Units described in this Grant Notice (the "***RSUs***"), subject to the terms and conditions of the Plan and the Restricted Share Unit Agreement attached as **Exhibit A** (the "***Agreement***"), both of which are incorporated into this Grant Notice by reference.

Participant:

Grant Date:

Number of RSUs:

Vesting Commencement Date:

Vesting Schedule: [To be specified in individual award agreements]

By Participant's signature below, Participant agrees to be bound by the terms of this Grant Notice, the Plan and the Agreement. Participant has reviewed the Plan, this Grant Notice and the Agreement in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Grant Notice and fully understands all provisions of the Plan, this Grant Notice and the Agreement. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions arising under the Plan, this Grant Notice or the Agreement.

MEIRAGTX HOLDINGS PLC	**PARTICIPANT**
By: _____	_____
Name: _____	[Participant Name]
Title: _____	

Exhibit A

RESTRICTED SHARE UNIT AGREEMENT

Capitalized terms not specifically defined in this Agreement have the meanings specified in the Grant Notice or, if not defined in the Grant Notice, in the Plan.

ARTICLE I.
GENERAL

1.1 Award of RSUs and Dividend Equivalents.

(a) The Company has granted the RSUs to Participant effective as of the grant date set forth in the Grant Notice (the "***Grant Date***"). Each RSU represents the right to receive one Share or, at the option of the Company, an amount of cash, in either case, as set forth in this Agreement. Participant will have no right to the distribution of any Shares or payment of any cash until the time (if ever) the RSUs have vested.

(b) The Company hereby grants to Participant, with respect to each RSU, a Dividend Equivalent for ordinary cash dividends paid to substantially all holders of outstanding Shares with a record date after the Grant Date and prior to the date the applicable RSU is settled, forfeited or otherwise expires. Each Dividend Equivalent entitles Participant to receive the equivalent value of any such ordinary cash dividends paid on a single Share. The Company will establish a separate Dividend Equivalent bookkeeping account (a "***Dividend Equivalent Account***") for each Dividend Equivalent and credit the Dividend Equivalent Account (without interest) on the applicable dividend payment date with the amount of any such cash paid.

1.2 Incorporation of Terms of Plan. The RSUs are subject to the terms and conditions set forth in this Agreement and the Plan, which is incorporated herein by reference. In the event of any inconsistency between the Plan and this Agreement, the terms of the Plan will control.

1.3 Unsecured Promise. The RSUs and Dividend Equivalents will at all times prior to settlement represent an unsecured Company obligation payable only from the Company's general assets.

ARTICLE II.
VESTING; FORFEITURE AND SETTLEMENT

2.1 Vesting; Forfeiture. The RSUs will vest according to the vesting schedule in the Grant Notice except that any fraction of an RSU that would otherwise be vested will be accumulated and will vest only when a whole RSU has accumulated. In the event of Participant's Termination of Service for any reason, all unvested RSUs will immediately and automatically be cancelled and forfeited, except as otherwise determined by the Administrator or provided in a binding written agreement between Participant and the Company. Dividend Equivalents (including any Dividend Equivalent Account balance) will vest or be forfeited, as applicable, upon the vesting or forfeiture of the RSU with respect to which the Dividend Equivalent (including the Dividend Equivalent Account) relates.

2.2 Settlement.

(a) RSUs and Dividend Equivalents (including any Dividend Equivalent Account balance) will be paid in Shares or cash at the Company's option as soon as administratively practicable after the vesting of the applicable RSU, but in no event more than sixty (60) days after the RSU's vesting date. Notwithstanding the foregoing, the Company may delay any payment under this Agreement that the Company reasonably determines would violate Applicable Law until the earliest date the Company

reasonably determines the making of the payment will not cause such a violation (in accordance with Treasury Regulation Section 1.409A-2(b)(7)(ii)), provided the Company reasonably believes the delay will not result in the imposition of excise taxes under Section 409A.

(b) If an RSU is paid in cash, the amount of cash paid with respect to the RSU will equal the Fair Market Value of a Share on the day immediately preceding the payment date. If a Dividend Equivalent is paid in Shares, the number of Shares paid with respect to the Dividend Equivalent will equal the quotient, rounded down to the nearest whole Share, of the Dividend Equivalent Account balance divided by the Fair Market Value of a Share on the day immediately preceding the payment date.

ARTICLE III.
TAXATION AND TAX WITHHOLDING

3.1 Representation. Participant represents to the Company that Participant has reviewed with Participant's own tax advisors the tax consequences of this Award and the transactions contemplated by the Grant Notice and this Agreement. Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents.

3.2 Tax Withholding.

(a) Notwithstanding Section 9.5 of the Plan, unless the Administrator otherwise determines, any withholding tax obligation arising in connection with the RSUs or Dividend Equivalents shall be satisfied by the Company's retaining from Shares otherwise issuable under the Award the minimum number of whole Shares, valued at their Fair Market Value as of the time the tax withholding obligation arises, that is sufficient to satisfy such tax withholding obligation based on applicable statutory withholding rates.

(b) Participant acknowledges that Participant is ultimately liable and responsible for all taxes owed in connection with the RSUs and the Dividend Equivalents, regardless of any action the Company or any Subsidiary takes with respect to any tax withholding obligations that arise in connection with the RSUs or Dividend Equivalents. Neither the Company nor any Subsidiary makes any representation or undertaking regarding the treatment of any tax withholding in connection with the awarding, vesting or payment of the RSUs or the Dividend Equivalents or the subsequent sale of Shares. The Company and the Subsidiaries do not commit and are under no obligation to structure the RSUs or Dividend Equivalents to reduce or eliminate Participant's tax liability.

ARTICLE IV.
OTHER PROVISIONS

4.1 Adjustments. Participant acknowledges that the RSUs, the Shares subject to the RSUs and the Dividend Equivalents are subject to adjustment, modification and termination in certain events as provided in this Agreement and the Plan.

4.2 Notices. Any notice to be given under the terms of this Agreement to the Company must be in writing and addressed to the Company in care of the Company's Secretary at the Company's principal office or the Secretary's then-current email address or facsimile number. Any notice to be given under the terms of this Agreement to Participant must be in writing and addressed to Participant at Participant's last known mailing address, email address or facsimile number in the Company's personnel files. By a notice given pursuant to this Section, either party may designate a different address for notices to be given to that party. Any notice will be deemed duly given when actually received, when sent by email, when sent by certified mail (return receipt requested) and deposited with postage prepaid in a post office or branch post

office regularly maintained by the United States Postal Service, when delivered by a nationally recognized express shipping company or upon receipt of a facsimile transmission confirmation.

4.3 Titles. Titles are provided herein for convenience only and are not to serve as a basis for interpretation or construction of this Agreement.

4.4 Conformity to Securities Laws. Participant acknowledges that the Plan, the Grant Notice and this Agreement are intended to conform to the extent necessary with all Applicable Laws and, to the extent Applicable Laws permit, will be deemed amended as necessary to conform to Applicable Laws.

4.5 Successors and Assigns. The Company may assign any of its rights under this Agreement to single or multiple assignees, and this Agreement will inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer set forth in the Plan, this Agreement will be binding upon and inure to the benefit of the heirs, legatees, legal representatives, successors and assigns of the parties hereto.

4.6 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the Plan or this Agreement, if Participant is subject to Section 16 of the Exchange Act, the Plan, the Grant Notice, this Agreement, the RSUs and the Dividend Equivalents will be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3) that are requirements for the application of such exemptive rule. To the extent Applicable Laws permit, this Agreement will be deemed amended as necessary to conform to such applicable exemptive rule.

4.7 Entire Agreement. The Plan, the Grant Notice and this Agreement (including any exhibit hereto) constitute the entire agreement of the parties and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof.

4.8 Agreement Severable. In the event that any provision of the Grant Notice or this Agreement is held illegal or invalid, the provision will be severable from, and the illegality or invalidity of the provision will not be construed to have any effect on, the remaining provisions of the Grant Notice or this Agreement.

4.9 Limitation on Participant's Rights. Participation in the Plan confers no rights or interests other than as herein provided. This Agreement creates only a contractual obligation on the part of the Company as to amounts payable and may not be construed as creating a trust. Neither the Plan nor any underlying program, in and of itself, has any assets. Participant will have only the rights of a general unsecured creditor of the Company with respect to amounts credited and benefits payable, if any, with respect to the RSUs and Dividend Equivalents, and rights no greater than the right to receive cash or the Shares as a general unsecured creditor with respect to the RSUs and Dividend Equivalents, as and when settled pursuant to the terms of this Agreement.

4.10 Not a Contract of Employment. Nothing in the Plan, the Grant Notice or this Agreement confers upon Participant any right to continue in the employ or service of the Company or any Subsidiary or interferes with or restricts in any way the rights of the Company and its Subsidiaries, which rights are hereby expressly reserved, to discharge or terminate the services of Participant at any time for any reason whatsoever, with or without Cause, except to the extent expressly provided otherwise in a written agreement between the Company or a Subsidiary and Participant.

4.11 Counterparts. The Grant Notice may be executed in one or more counterparts, including by way of any electronic signature, subject to Applicable Law, each of which will be deemed an original and all of which together will constitute one instrument.

4.12 Electronic Delivery and Acceptance. The Company may, in its sole discretion, decide to deliver any documents related to current or future participation in the Plan by electronic means. Participant hereby consents to receive such documents by electronic delivery and agrees to participate in the Plan through an on-line or electronic systems established and maintained by the Company or a third party designated by the Company.

4.13 Deemed Acceptance. Participant is required to accept the terms and conditions set forth in this Agreement prior to the first vesting date in order for Participant to receive the RSUs granted hereunder. If Participant wishes to decline the RSUs, Participant must reject this Agreement prior to the first vesting date. For Participant's benefit, if Participant has not rejected the Agreement prior to the first vesting date, Participant will be deemed to have automatically accepted the RSUs and all the terms and conditions set forth in this Agreement. Deemed acceptance will allow the shares to be released to Participant in a timely manner and once released, Participant waives any right to assert that Participant has not accepted the terms hereof.

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MEIRAGTX HOLDINGS PLC
2018 INCENTIVE AWARD PLAN UK SUB-PLAN

RESTRICTED SHARE UNIT GRANT NOTICE FOR UK PARTICIPANTS

Capitalized terms not specifically defined in this Restricted Share Unit Grant Notice for UK Participants (the "***Grant Notice***") have the meanings given to them in the 2018 Incentive Award Plan UK Sub-Plan (the "***UK Sub-Plan***") of MeiraGTx Holdings plc (the "***Company***"), which incorporates terms from the Company's 2018 Incentive Award Plan (the "***Plan***").

The Company has granted to the participant listed below ("***Participant***") the Restricted Share Units described in this Grant Notice (the "***RSUs***"), subject to the terms and conditions of the UK Sub-Plan and the Restricted Share Unit Agreement attached as **Exhibit A** (the "***UK RSU Agreement***"), both of which are incorporated into this Grant Notice by reference.

Participant:

Grant Date:

Number of RSUs:

Vesting Commencement Date:

Vesting Schedule: [To be specified in individual award agreements]

By Participant's signature below, Participant agrees to be bound by the terms of this Grant Notice, the UK Sub-Plan and the UK RSU Agreement. Participant has reviewed the UK Sub-Plan, this Grant Notice and the UK RSU Agreement in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Grant Notice and fully understands all provisions of the UK Sub-Plan, this Grant Notice and the UK RSU Agreement. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions arising under the UK Sub-Plan, this Grant Notice or the UK RSU Agreement.

MEIRAGTX HOLDINGS PLC	**PARTICIPANT**
By: _____	_____
Name: _____	[Participant Name]
Title: _____	

Exhibit A

RESTRICTED SHARE UNIT AGREEMENT FOR UK PARTICIPANTS

Capitalized terms not specifically defined in this UK RSU Agreement have the meanings specified in the Grant Notice or, if not defined in the Grant Notice, in the UK Sub-Plan.

ARTICLE I.
GENERAL

1.1 Award of RSUs and Dividend Equivalents.

(a) The Company has granted the RSUs to Participant effective as of the grant date set forth in the Grant Notice (the "***Grant Date***"). Each RSU represents the right to receive one Share or, at the option of the Company, an amount of cash, in either case, as set forth in this UK RSU Agreement. Participant will have no right to the distribution of any Shares or payment of any cash until the time (if ever) the RSUs have vested.

(b) The Company hereby grants to Participant, with respect to each RSU, a Dividend Equivalent for ordinary cash dividends paid to substantially all holders of outstanding Shares with a record date after the Grant Date and prior to the date the applicable RSU is settled, forfeited or otherwise expires. Each Dividend Equivalent entitles Participant to receive the equivalent value of any such ordinary cash dividends paid on a single Share. The Company will establish a separate Dividend Equivalent bookkeeping account (a "***Dividend Equivalent Account***") for each Dividend Equivalent and credit the Dividend Equivalent Account (without interest) on the applicable dividend payment date with the amount of any such cash paid.

1.2 Incorporation of Terms of UK Sub-Plan. The RSUs are subject to the terms and conditions set forth in this UK RSU Agreement and the UK Sub-Plan, which is incorporated herein by reference. In the event of any inconsistency between the UK Sub-Plan and this UK RSU Agreement, the terms of the UK RSU Agreement will control.

1.3 Unsecured Promise. The RSUs and Dividend Equivalents will at all times prior to settlement represent an unsecured Company obligation payable only from the Company's general assets.

ARTICLE II.
VESTING; FORFEITURE AND SETTLEMENT

2.1 Vesting; Forfeiture. The RSUs will vest according to the vesting schedule in the Grant Notice except that any fraction of an RSU that would otherwise be vested will be accumulated and will vest only when a whole RSU has accumulated. In the event of Participant's Termination of Service for any reason, all unvested RSUs will immediately and automatically be cancelled and forfeited, except as otherwise determined by the Administrator or provided in a binding written agreement between Participant and the Company. Dividend Equivalents (including any Dividend Equivalent Account balance) will vest or be forfeited, as applicable, upon the vesting or forfeiture of the RSU with respect to which the Dividend Equivalent (including the Dividend Equivalent Account) relates.

2.2 Settlement.

(a) RSUs and Dividend Equivalents (including any Dividend Equivalent Account balance) will be paid in Shares or cash at the Company's option as soon as administratively practicable after the vesting of the applicable RSU, but in no event more than sixty (60) days after the RSU's vesting date. Notwithstanding the foregoing, the Company may delay any payment under this UK RSU Agreement

that the Company reasonably determines would violate Applicable Law until the earliest date the Company reasonably determines the making of the payment will not cause such a violation (in accordance with Treasury Regulation Section 1.409A-2(b)(7)(ii), if applicable), provided the Company reasonably believes the delay will not result in the imposition of excise taxes under Section 409A.

(b) If an RSU is paid in cash, the amount of cash paid with respect to the RSU will equal the Fair Market Value of a Share on the day immediately preceding the payment date. If a Dividend Equivalent is paid in Shares, the number of Shares paid with respect to the Dividend Equivalent will equal the quotient, rounded down to the nearest whole Share, of the Dividend Equivalent Account balance divided by the Fair Market Value of a Share on the day immediately preceding the payment date.

ARTICLE III.
TAXATION AND TAX WITHHOLDING

3.1 Representation. Participant represents to the Company that Participant has reviewed with Participant's own tax advisors the tax consequences of this Award and the transactions contemplated by the Grant Notice and this UK RSU Agreement. Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents.

3.2 UK Tax Obligations.

(a) Tax Indemnity. Participant agrees to indemnify and keep indemnified the Company and his/her employing company ("***Employer***"), if different, from and against any liability for or obligation to pay any Tax Liability (a "***Tax Liability***" being any liability for income tax, employee's National Insurance contributions and (at the discretion of the Company) employer's National Insurance Contributions (or other similar obligations to pay tax and social security wherever in the world arising)) that is attributable to: (1) the grant or vesting, or any benefit derived by Participant from, the RSUs or the Shares which are the subject of the RSUs or Dividend Equivalents; (2) the transfer or issue of Shares to Participant on settlement of the RSUs or Dividend Equivalents or any other benefit on settlement of the RSUs or Dividend Equivalents; (3) any restrictions applicable to the Shares held by the Participant ceasing to apply to those shares; or (4) the disposal of any Shares.

(b) Tax Liability. The Company shall not be required to issue, allot or transfer Shares until Participant has satisfied any Tax Liability that may arise in connection with the settlement of the RSUs or Dividend Equivalents and/or the acquisition of the Shares by the Participant. Notwithstanding Section 9.5 of the Plan (as modified by the UK Sub-Plan), unless the Administrator otherwise determines, any Tax Liability shall be satisfied by the Company's retaining from Shares otherwise issuable under the Award the minimum number of whole Shares, valued at their Fair Market Value as of the time the Tax Liability arises, that is sufficient to satisfy such Tax Liability based on applicable statutory withholding rates.

(c) Election. Participant undertakes that, upon request by the Company, he/she will (on or within 14 days of acquiring the Shares) join with his/her Employer in electing, pursuant to Section 431(1) of the Income Tax (Earnings and Pensions) Act 2003 ("***ITEPA***") that, for relevant tax purposes, the market value of the Shares acquired on settlement of the RSUs or Dividend Equivalents on any occasion will be calculated as if the Shares were not restricted and Sections 425 to 430 (inclusive) of ITEPA are not to apply to such Shares.

(d) Acknowledgement. Participant acknowledges that Participant is ultimately liable and responsible for all taxes owed in connection with the RSUs and the Dividend Equivalents, regardless of any action the Company or any Subsidiary takes with respect to any tax withholding obligations that arise in connection with the RSUs or Dividend Equivalents. Neither the Company nor any Subsidiary

makes any representation or undertaking regarding the treatment of any tax withholding in connection with the awarding, vesting or payment of the RSUs or the Dividend Equivalents or the subsequent sale of Shares. The Company and the Subsidiaries do not commit and are under no obligation to structure the RSUs or Dividend Equivalents to reduce or eliminate Participant's Tax Liability.

ARTICLE IV.
OTHER PROVISIONS

4.1 Adjustments. Participant acknowledges that the RSUs, the Shares subject to the RSUs and the Dividend Equivalents are subject to adjustment, modification and termination in certain events as provided in this UK RSU Agreement and the UK Sub-Plan.

4.2 Notices. Any notice to be given under the terms of this UK RSU Agreement to the Company must be in writing and addressed to the Company in care of the Company's Secretary at the Company's principal office or the Secretary's then-current email address or facsimile number. Any notice to be given under the terms of this UK RSU Agreement to Participant must be in writing and addressed to Participant at Participant's last known mailing address, email address or facsimile number in the Company's personnel files. By a notice given pursuant to this Section, either party may designate a different address for notices to be given to that party. Any notice will be deemed duly given when actually received, when sent by email, when sent by certified mail (return receipt requested) and deposited with postage prepaid in a post office or branch post office regularly maintained by the United States Postal Service, when delivered by a nationally recognized express shipping company or upon receipt of a facsimile transmission confirmation.

4.3 Titles. Titles are provided herein for convenience only and are not to serve as a basis for interpretation or construction of this UK RSU Agreement.

4.4 Conformity to Securities Laws. Participant acknowledges that the UK Sub-Plan, the Grant Notice and this UK RSU Agreement are intended to conform to the extent necessary with all Applicable Laws and, to the extent Applicable Laws permit, will be deemed amended as necessary to conform to Applicable Laws.

4.5 Successors and Assigns. The Company may assign any of its rights under this UK RSU Agreement to single or multiple assignees, and this UK RSU Agreement will inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer set forth in the UK Sub-Plan, this UK RSU Agreement will be binding upon and inure to the benefit of the heirs, legatees, legal representatives, successors and assigns of the parties hereto.

4.6 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the UK Sub-Plan or this UK RSU Agreement, if Participant is subject to Section 16 of the Exchange Act, the UK Sub-Plan, the Grant Notice, this UK RSU Agreement, the RSUs and the Dividend Equivalents will be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3) that are requirements for the application of such exemptive rule. To the extent Applicable Laws permit, this UK RSU Agreement will be deemed amended as necessary to conform to such applicable exemptive rule.

4.7 Entire Agreement. The UK Sub-Plan, the Grant Notice and this UK RSU Agreement (including any exhibit hereto) constitute the entire agreement of the parties and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof.

4.8 Agreement Severable. In the event that any provision of the Grant Notice or this UK RSU Agreement is held illegal or invalid, the provision will be severable from, and the illegality or invalidity of the provision will not be construed to have any effect on, the remaining provisions of the Grant Notice or this UK RSU Agreement.

4.9 Limitation on Participant's Rights. Participation in the UK Sub-Plan confers no rights or interests other than as herein provided. This UK RSU Agreement creates only a contractual obligation on the part of the Company as to amounts payable and may not be construed as creating a trust. Neither the UK Sub-Plan nor any underlying program, in and of itself, has any assets. Participant will have only the rights of a general unsecured creditor of the Company with respect to amounts credited and benefits payable, if any, with respect to the RSUs and Dividend Equivalents, and rights no greater than the right to receive cash or the Shares as a general unsecured creditor with respect to the RSUs and Dividend Equivalents, as and when settled pursuant to the terms of this UK RSU Agreement.

4.10 Not a Contract of Employment. Nothing in the UK Sub-Plan, the Grant Notice or this UK RSU Agreement confers upon Participant any right to continue in the employ or service of the Company or any Subsidiary or interferes with or restricts in any way the rights of the Company and its Subsidiaries, which rights are hereby expressly reserved, to discharge or terminate the services of Participant at any time for any reason whatsoever, with or without Cause, except to the extent expressly provided otherwise in a written agreement between the Company or a Subsidiary and Participant.

4.11 Counterparts. The Grant Notice may be executed in one or more counterparts, including by way of any electronic signature, subject to Applicable Law, each of which will be deemed an original and all of which together will constitute one instrument.

4.12 Data Protection. The Company and all its Subsidiaries may transfer, collect, use, process or disclose, in electronic or other form, such information to third parties, including where they are situated outside the European Economic Area in countries where the level of data protection may not be as high as in the Participant's country of residence, in the event that such disclosure is in their view required for the performance of their obligations under the Plan. The Company and all Group Companies shall ensure that such collection, use, processing and transfers are made in accordance with the EU General Data Protection Regulation and other applicable data protection laws in any other jurisdiction.

4.13 Acknowledgement. Participant acknowledges that neither this UK RSU Agreement nor the UK Sub-Plan has been issued, nor has it been approved by, an authorised person within the meaning of the Financial Services and Markets Act 2000 of the United Kingdom and is being directed at the Participant because the offer to which this UK RSU Agreement and the UK Sub-Plan relate has been determined as having regard to the Participant's circumstances as an employee of the Company. This UK RSU Agreement is strictly confidential and is not for distribution to, and may not be acted upon by, any other person other than the person to whom it has been specifically addressed.

4.14 Electronic Delivery and Acceptance. The Company may, in its sole discretion, decide to deliver any documents related to current or future participation in the Plan by electronic means. Participant hereby consents to receive such documents by electronic delivery and agrees to participate in the Plan through an on-line or electronic systems established and maintained by the Company or a third party designated by the Company.

4.15 Deemed Acceptance. Participant is required to accept the terms and conditions set forth in this Agreement prior to the first vesting date in order for Participant to receive the RSUs granted hereunder. If Participant wishes to decline the RSUs, Participant must reject this Agreement prior to the first vesting date. For Participant's benefit, if Participant has not rejected the Agreement prior to the first vesting date,

Participant will be deemed to have automatically accepted the RSUs and all the terms and conditions set forth in this Agreement. Deemed acceptance will allow the shares to be released to Participant in a timely manner and once released, Participant waives any right to assert that Participant has not accepted the terms hereof.

*** * * * ***

Exhibit 21

SUBSIDIARIES OF MEIRAGTX HOLDINGS PLC

Legal Name of Subsidiary	**Jurisdiction of Organization**
BRI-Alzan, Inc.	Delaware
MeiraGTx B.V.	Netherlands
Arthrogen B.V.	Netherlands
MeiraGTx Limited	England and Wales
MeiraGTx, LLC	Delaware
MeiraGTx UK Limited	England and Wales
MeiraGTx UK II Limited	England and Wales
MeiraGTx Neurosciences, Inc.	Delaware

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-225535) pertaining to the 2016 Equity Incentive Plan, 2018 Incentive Award Plan and 2018 Employee Share Purchase Plan of MeiraGTx Holdings plc,

(2) Registration Statement (Form S-3 No. 333-232527) of MeiraGTx Holdings plc, and

(3) Registration Statement (Form S-3 No. 333-232677) of MeiraGTx Holdings plc;

of our report dated March 11, 2020, with respect to the consolidated financial statements of MeiraGTx Holdings plc included in this Annual Report (Form 10-K) of MeiraGTx Holdings plc for the year ended December 31, 2019.

/s/ Ernst & Young LLP

Stamford, Connecticut
March 11, 2020

Exhibit 31.1

CERTIFICATION

I, Alexandria Forbes, certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2019 of MeiraGTx Holdings plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2020

By: /s/ Alexandria Forbes

Alexandria Forbes
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Richard Giroux, certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2019 of MeiraGTx Holdings plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2020

By: /s/ Richard Giroux

Richard Giroux
Chief Financial Officer and Chief Operating Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of MeiraGTx Holdings plc (the "Company") for the year ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 11, 2020

By: /s/ Alexandria Forbes

Alexandria Forbes
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of MeiraGTx Holdings plc (the "Company") for the year ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 11, 2020

By: /s/ Richard Giroux

Richard Giroux
Chief Financial Officer and Chief Operating Officer
(Principal Financial Officer)