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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, 2020
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)	**98-1448305** (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 par value per share	**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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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 30, 2020, 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 $284,754,241 (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, 2021, the registrant had 44,264,150 ordinary shares outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2021 annual shareholder meeting to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2020 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.

RISK FACTOR SUMMARY

We are providing the following summary of the principal risk factors contained in this Form 10-K to enhance the readability and accessibility of our risk factor disclosures. We encourage you to carefully review in their entirety the full risk factors set forth in the section of this Form 10-K captioned "Item 1A. Risk Factors" for additional information regarding the material factors that make an investment in our ordinary shares speculative or risky. These risks and uncertainties include, among others, the following:

- We have incurred significant losses since inception and anticipate that we will incur continued losses for the foreseeable future, and may never achieve or maintain profitability.
- We will require additional capital to fund our operations, which may not be available on acceptable terms, if at all.
- We are heavily dependent on the success of our Most Advanced Product Candidates (as defined in "Item 1A. Risk Factors"), which are still in development, and if none of them receive regulatory approval or are successfully commercialized, our business may be harmed.
- The outbreak of the novel coronavirus disease, COVID-19, or other pandemic, epidemic or outbreak of an infectious disease may materially and adversely impact our business, including our preclinical studies and clinical trials.
- 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 gene therapies have been approved in the United States or in Europe.
- Because gene therapy is novel and the regulatory landscape that governs any product candidates we may develop is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.
- Clinical trials are expensive, time-consuming, difficult to design and implement, and involve an uncertain outcome. Further, we may encounter substantial delays in our clinical trials.
- The affected populations for our product candidates may be smaller than we or third parties currently project, which may affect the addressable markets for our product candidates.
- We and our contract manufacturers for plasmid are subject to significant regulation with respect to manufacturing our products. Our manufacturing facilities and the third-party manufacturing facilities which we rely on may not continue to meet regulatory requirements and have limited capacity.
- 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.
- 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 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.

- 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.
- 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 will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.
- Our future success depends on our ability to retain our key personnel and to attract, retain and motivate qualified personnel.

BASIS OF PRESENTATION

Unless the context otherwise requires, references in this Form 10-K to "Meira," "MeiraGTx," "we," "us", "our" or "the Company" refer to MeiraGTx Holdings plc and its subsidiaries.

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 in London, United Kingdom 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. The MHRA re-certified the facility in the second quarter of 2020.

We have expanded our manufacturing capabilities by acquiring a second cGMP viral vector manufacturing facility and a cGMP plasmid and DNA production facility in Shannon, Ireland. We completed the acquisition of these facilities in January 2021. The campus encompasses 150,000 square feet and will include a high capacity cGMP manufacturing hub, clinical supply storage, quality control laboratories for global release, up to ten viral vector production suites, fully scalable automated fill and finish facilities, an extensive warehouse and a separate cGMP plasmid and DNA manufacturing facility. We believe building our second viral vector manufacturing facility and bringing cGMP plasmid and DNA 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: ocular diseases, including inherited retinal diseases, or IRDs, as well as large degenerative diseases, 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, 2021 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.

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;
- other ocular conditions— glaucoma and uveitis;

- 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;

- central nervous systems/peripheral nervous system diseases—brain-derived neurotrophic factor gene therapy for treatment of genetic obesity disorders, as well as the development of gene therapy product candidates for other central nervous system diseases;

- 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/autoimmune diseases—use of gene therapy technology for the local delivery of immunomodulatory therapeutics, including osteoarthritis, gout and certain rare inflammatory disorders.

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, 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, glaucoma and uveitis, as well as several other IRDs including retinol dehydrogenase 12, or RDH12, mutation-associated retinal dystrophy.

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 disclosed six-month data from the dose escalation portion of the study as a late-breaker at the American Society of Retina Specialists 2020 Virtual Annual Meeting in July 2020, nine-month data at EURETINA 2020 Virtual Congress in October 2020 and twelve-month data at the American Academy of Ophthalmology 2020 Virtual Annual Meeting in November 2020. Data from each time point revealed that patients treated with low (n=3) and intermediate (n=4) dose AAV-RPGR experienced statistically significant improvement in retinal sensitivity. Nine-month data also indicated significant improvement in vision-guided mobility, and at 12-months, six of seven patients continued to show improved or stable vision in the treated eye. Each patient was treated with subretinal delivery of AAV-RPGR in one eye and the patient's other eye served as an untreated control. The primary endpoint of the trial is safety, with secondary endpoints assessing changes in visual function at pre-specified timepoints post-treatment. Baseline values were determined in triplicate. We also announced in July 2020 that based on the data from those dose escalation cohorts, we anticipate initiating in 2021 the Phase 3 Lumeos clinical trial of AAV-RPGR for the treatment of patients with XLRP caused by mutations in the *RPGR* gene. Additionally, based on the safety and efficacy profile, the low and intermediate doses are being evaluated in the ongoing randomized, controlled, extension portion of the Phase 1/2 study, which completed enrollment in the first half of 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), advanced therapy medicinal product (ATMP) 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 has 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 expect to initiate a Phase 3 clinical trial for AAV-RPE65 in the second half of 2021.

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 are currently conducting an open-label, dose-escalation Phase 1/2 clinical trial of AAV-CNGA3 in patients with ACHM due to mutations in the *CNGA3* gene.

Our gene therapy product candidate AAV-CNGA3 was granted orphan drug designation by the FDA and EMA, rare pediatric disease designation by the FDA, and in January 2021, was granted Fast Track designation by the FDA for the treatment of achromatopsia caused by *CNGA3* mutations.

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.

We have manufactured and released AAV-AIPL1 for compassionate use under an MHRA specials license in the UK to treat LCA4 patients. A specials license 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 any 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 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.

AAV-RDH12 for the Treatment of RDH12 Mutation-Associated Retinal Dystrophy

Disease-causing sequence variants in RDH12 cause severe retinal dystrophy most often resulting in the clinical diagnosis of Leber congenital amaurosis (LCA) and early onset severe retinal dystrophy (EOSRD); although RDH12 variants have also been associated with a clinical diagnosis of RP. Sequence variants in RDH12 account for 3.4%–10.5% of LCA/EOSRD. Individuals with RDH12 deficiency exhibit widespread retinal degeneration impacting both rods and cones, with early macular involvement. Most people with RDH12–LCA/EOSRD experience marked central visual loss by their late teens to twenties. AAV-RDH12 is an AAV based gene therapy designed to deliver a functional copy of the RDH12 gene to the retina of patients with genetically defined RDH12 deficiency.

We recently received orphan drug designation from the FDA as well as orphan medicinal product designation from the EMA for AAV-RDH12.

Wet and Dry Neovascular Age Related Macular Degeneration (AMD)

We are developing pre-clinical programs relating 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 650,000 new cases of head and neck cancer diagnosed each year, with approximately 58,000 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 15,000 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 infrared radiation 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 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 have treated one patient in our second cohort. We expect to continue to open additional sites and enroll patients in dose escalation cohorts throughout 2021. In December 2020, we provided an update on the first cohort of patients (n=3) treated in this clinical trial where one patient has reached the 12-month assessment and two have passed the 6-month assessment. In these patients, AAV-hAQP1 has been well tolerated with no dose limiting toxicity and no serious adverse events reported. Encouraging responses have been seen in both patient-reported measures of xerostomia symptoms and in salivary output in the patients treated in this first cohort, with complete resolution of symptoms in the patient who has reached the 12-month timepoint. Based on the encouraging safety and tolerability profile from this first cohort, we are initiating plans for a Phase 2 efficacy and safety clinical trial for the treatment of patients with radiation-induced xerostomia.

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 anticipate filing an Investigational New Drug application (IND) for AAV-GAD by the third quarter of 2021, with material that has been manufactured with our in-house proprietary manufacturing process at our cGMP manufacturing facility in London.

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 in London, 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 have also expanded our manufacturing capabilities by acquiring a second cGMP viral vector manufacturing facility and cGMP plasmid and DNA production facility in Shannon, Ireland. The plasmid and DNA production facility is complete and we expect the viral vector manufacturing facility to be completed during 2021.

- **Robust and Diverse Clinical and Preclinical Pipeline:** Applying our portfolio approach to gene therapy product development, our initial focus is on treatments for ocular disorders, including IRDs, as well as 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.

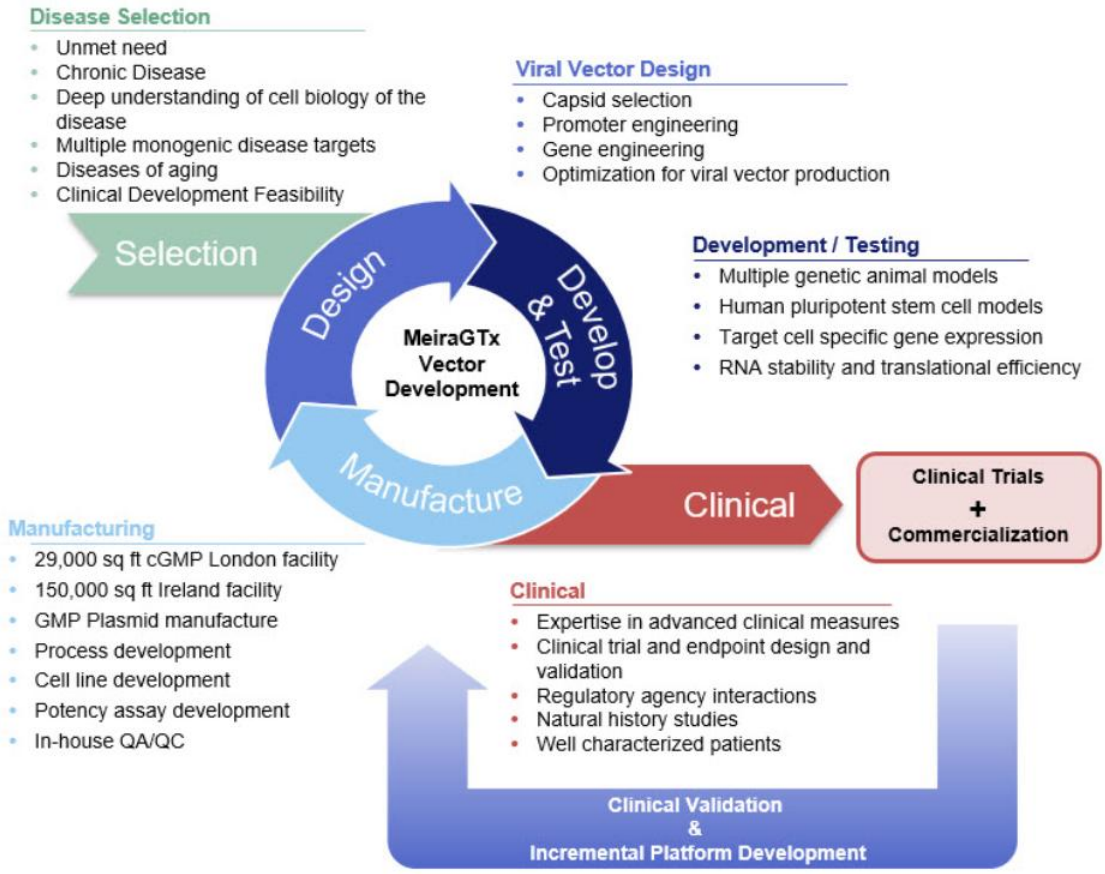
Our Strategy

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. In recent years, 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: Vector Engineering, Natural History Studies and Relationships with Leading Institutions

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 (including the UK), affected by IRDs. However, IRDs may be caused by mutations in over 300 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 5,000x 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 London 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 London 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. It is also 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 120 highly trained multidisciplinary staff on our manufacturing team with backgrounds in a diverse array of manufacturing sciences, technologies, analytics and production working together to expedite delivery of gene therapy products.

We have identified and licensed a proprietary HEK-293 cell line that is well characterized and that we have banked in hundreds of 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 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 have expanded our manufacturing capabilities by acquiring a second cGMP viral vector manufacturing facility and a cGMP plasmid and DNA production facility in Shannon, Ireland. We completed the acquisition of these facilities in January 2021. The campus encompasses 150,000 square feet and will include a high capacity cGMP manufacturing hub, clinical supply storage, quality control laboratories for global release, up to ten viral vector production suites, fully scalable automated fill and finish facilities, an extensive warehouse and a separate cGMP plasmid and DNA manufacturing facility.

We currently rely on third-party manufacturers for the plasmid used in the production of our product candidates. We believe that building a second viral vector manufacturing facility and bringing cGMP plasmid and DNA production in-house will provide greater flexibility and efficiency as we advance our product candidates through development, and should they be approved, commercial production. The plasmid and DNA production facility has been completed and we expect the vital vector facility to be completed by the end of 2021.

Our significant investment in the development of our internal manufacturing capacity and expertise to allow for better control over our process development timelines, costs, product quality and intellectual property provides us with a key competitive advantage.

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 each of Biogen Inc. and 4D Molecular Therapeutics, 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, 2020, we own, co-own, have an exclusive license, or an exclusive option to license 200 United States and foreign issued or allowed patents and 321 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 Biologics License Application.

Company-Owned Intellectual Property

We own six patent families relating to gene regulation platform technologies developed by us. The first patent family includes one issued patent in the United States and 23 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 (two applications). 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 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 on March 2, 2038, not including any patent term adjustments that may extend the patent term in certain jurisdictions.

The sixth 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 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 80 United States and foreign issued patents and 68 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 39 issued patents in the Unites States, Singapore, Albania, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Monaco, the Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, San Moreno, Serbia, Slovenia, Slovakia, Spain, Sweden, Switzerland, Turkey, and the United Kingdom and 17 pending patent applications in the United States, Europe, Australia, Canada, China, Hong Kong, India, Japan, Brazil, Egypt, Israel, Malaysia, Mexico, New Zealand, Nigeria, Philippines, 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 includes 22 pending patent applications with claims directed to compositions of matter and methods of use relating to our achromatopsia program and the AAV-CNGA3 product candidate 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 January 14, 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 39 issued patent applications in the United States, Japan, Albania, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Monaco, the Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, San Moreno, Serbia, Slovenia, Slovakia, Spain, Sweden, Switzerland, Turkey, and the United Kingdom and five pending applications in the United States, Europe, Canada, China, and Japan. Patents issued from this family are expected to expire July 15, 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 two issued patents in Japan and Singapore and 24 pending applications in the United States, Europe, Australia, Canada, China, Hong Kong (two applications), India, 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 15 issued patents in the United States, Australia, Austria, Belgium, Denmark, France, Germany, Ireland, Italy, Netherlands, Norway, Spain, Sweden, Switzerland, and the United Kingdom and five pending patent applications in the United States, Europe, Canada and Hong Kong (two applications). 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 patents in the United States, Canada, Australia, Austria, Belgium, Denmark, France, Germany, Ireland, Italy, Netherlands, Norway, Spain, Sweden, Switzerland and the United Kingdom. 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 a 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 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 the sellers of 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 the sellers of 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.

U.S. Biological Products Development Process

Our 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 investigational new drug application, or IND, 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.

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, are subject to evaluation and assessment by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution, pursuant to the National Institutes of Health's Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. 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.

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 some 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.

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 PHSA 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.

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 is also subject to an initial 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. The FDA's goal is to complete the review of standard BLAs within ten months after it accepts an application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification.

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. 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 a 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.

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 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, or Breakthrough Therapy Designation. An application seeking marketing approval for a biologic product is eligible for priority review if the biologic has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or there is 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

Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP requirements. 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.

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.

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.

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.

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.

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, which may constrain the financial arrangements and relationships through which we conduct our research, as well as, sell, market and distribute any products for which we obtain marketing approval. Such laws include, without limitation, federal and state anti-kickback, fraud and abuse, false claims, data privacy and security and physician and other healthcare provider payment transparency laws and regulations. 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, administrative, civil and criminal penalties, damages, fines, disgorgement, 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 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. For example, the Tax Cuts and Jobs Act of 2017 was enacted, which, among other things, removed 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. 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. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review this case. The Supreme Court heard the case in November 2020, with a decision expected by June 2021. It is unclear how this decision or other efforts, if any, to challenge, repeal or replace the ACA will impact the law.

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, which was temporarily suspended from May 1, 2020 through March 31, 2021, 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. The likelihood of implementation of any of these reform initiatives is uncertain, particularly in light of the new Biden administration. 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. Data Privacy and Security

In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws, and federal and state consumer protection laws and regulations (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. For example, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, impose obligations on "covered entities," including certain health care providers, health plans, and health care clearinghouses,

and their respective "business associates" that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, as well as their covered subcontractors with respect to safeguarding the privacy, security and transmission of individually identifiable health information. In addition, certain state laws govern the privacy and security of personal information, including health-related 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. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

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. In addition, ethical, social and legal concerns about gene therapy, genetic testing, genetic research and gene-editing technology, could result in additional regulations restricting or prohibiting the processes we may use.

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. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. 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

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, or EU, 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 by the national health authority and the ethics committee has granted a positive opinion in relation to the conduct of the trial in the relevant member state(s) in accordance with a country's requirements, clinical trial development may proceed.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization, or ICH, guidelines on GCPs, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of ATMPs. If the sponsor of the clinical trial is not established within the EU, it must appoint an entity within the EU 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 CTA 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 CTA 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 GMP. Other national and EU-wide regulatory requirements may also apply.

During the development of a medicinal product, the EMA and national regulators within the EU 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

In the EU, medicinal products can only be placed on the market after obtaining a Marketing Authorization, or MA. To obtain regulatory approval of an investigational biological product in the EU, we must submit a marketing authorization application, or MAA. The application used to file the BLA in the United States is similar to that required in the EU, 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 MA, issued by the European Commission, based on the opinion of the CHMP of the EMA which is valid across the entire territory of the EU. 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) 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 an MAA 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 an MAA; 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, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days. This excludes so-called clock stops, during which additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. At the end of the review period, the CHMP provides an opinion to the European Commission. If this opinion is favorable, the Commission may then adopt a decision to grant an MA.

MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the European Commission or the national competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal

In exceptional cases, the CHMP might perform an accelerated review of an MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the Breakthrough Therapy Designation in the U.S. 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 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.

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 MA. Such conditional MAs 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 MA may contain specific obligations to be fulfilled by the MA holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional MAs 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 MA can be converted into a standard MA once the MA holder fulfils the obligations that were imposed and the complete data confirm that the medicine's benefits continue to outweigh its risks. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional MA.

The European Commission may also grant a so-called "marketing authorization under exceptional circumstances". Such MA 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 even after the product has been authorized, 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, MAs 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 MA 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 MA being suspended or revoked. The renewal of a MA of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" MA. Thus, a MA 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 MA under exceptional circumstances should not be granted when a conditional MA is more appropriate.

The EU 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 EU also provides opportunities for market exclusivity. MAAs 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 MA of a reference product for which regulatory data exclusivity has expired. Upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic or biosimilar 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 or biosimilar product can be marketed until the expiration of the market exclusivity. The overall ten-year market exclusivity period may be extended to a maximum of eleven years if during the first eight years a new therapeutic indication with significant clinical benefit over existing therapies is approved. 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 EU. 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 EU can receive ten years of market exclusivity. During the ten-year market exclusivity period once they are authorized as orphan medicines, the EMA cannot accept another application for a MA, or grant a MA or accept an application to extend an existing MA, for the same therapeutic indication, in respect of a similar medicinal product. An orphan medicinal product can also obtain an additional two years of market exclusivity in the EU 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 EU are similar in principle to those in the United States. 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 EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. 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 MA 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, a 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 Development

In the EU, MAAs for new medicinal products 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 study results are included in the product information, even when negative, the product is eligible for a six-months supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two year extension of the orphan market exclusivity is granted.

Post-Approval Requirements

Similar to the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a 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 MA. 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.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. 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 EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Iceland, Liechtenstein and Norway.

Pricing and Reimbursement

Even if a medicinal product obtains a MA in the EU, there can be no assurance that reimbursement for such product will be secured on a timely basis or at all. Governments influence the price of medicinal products 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. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. 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. In addition, in some countries, cross border imports from low-priced markets exert a commercial pressure on pricing within a country.

Rules Applicable in the United Kingdom

The UK formally left the EU on January 31, 2020, commonly referred to as "Brexit". The post-Brexit transition period, during which EU pharmaceutical laws continued to apply to the UK, expired on December 31, 2020. This means that since January 1, 2021, the UK operates under a distinct regulatory regime. EU pharmaceutical laws now only apply to the UK in respect of Northern Ireland (as laid out in the Protocol on Ireland and Northern Ireland, including but not limited to MAAs).

Since January 1, 2021, EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". As there is no general power to amend this "retained EU law", the UK government has introduced a new Medicines and Medical Devices Bill which seeks to address regulatory gaps through implementing regulations and delegated powers covering, among other things, the fields of human medicines and clinical trials of human medicines. The purpose of the bill is to enable the existing UK regulatory frameworks to be updated. Although regulatory authorities in the UK have indicated in the bill that new UK rules will closely align with EU laws, detailed proposals are yet to be published. The bill has not been formally enacted and had its final reading in the House of Lords on January 21, 2021. As the House of Lords proposed amendments to the draft legislation, the bill will go back to the other house of parliament for debate. There is no set time period for consideration of amendments and the bill will only proceed to be enacted as law once the draft bill has been agreed by both houses and royal assent has been obtained. The draft bill currently contemplates that the provisions will come into effect immediately upon enactment or otherwise within two months thereafter, with the exception of certain provisions on enforcement and disclosure, which are subject to further regulation. Significant political and economic uncertainty therefore remains about how much the relationship between the UK and EU will differ as a result of the UK's withdrawal.

On December 24, 2020 the EU and UK agreed to the EU-UK Trade and Cooperation Agreement, or TCA, which has been provisionally applicable since January 1, 2021. The TCA was ratified by the UK Parliament on December 30, 2020 and awaits final agreement of the EU member states. The TCA includes certain provisions affecting pharmaceutical companies such as customs and tariffs in relation to healthcare products and provides for the mutual recognition of Good Manufacturing Practice, or GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued. It is important to note that significant regulatory gaps still exist and the TCA does not contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards between the parties, for example, in relation to batch testing and pharmacovigilance which remain subject to further bilateral discussions.

UK Clinical Trials

The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation), and after Brexit, EU laws on clinical trials (including the impending EU Clinical Trials Regulation, EU CTR) are no longer directly applicable in Great Britain (i.e., the UK excluding Northern Ireland). There is a risk that the MHRA may diverge from the EU to maintain regulatory flexibility and changes impacting the ability to conduct trials spanning several EU countries will need to be closely monitored going forward. Already, as a result of Brexit various benefits of membership no longer apply to the UK such that, for example, UK sponsored trials that span several EU countries now need to have an individual or organization in the EU to act as a legal representative, or sponsor and it is unclear whether the UK will have access to new EU clinical trial databases such as the Clinical Trial Information System going forward (the centralized EU Portal for clinical trial information storage). Additionally, new rules apply to the import of investigational medicinal products from the EU and EEA to Great Britain.

UK Marketing Authorizations

The MHRA is now the UK's standalone regulator for MAAs. All existing centralized procedure MAs were automatically converted into UK MAs effective in Great Britain and issued with a UK MA number on January 1, 2021 (unless marketing authorization holders, or MAHs, opted out of this scheme by January 21, 2021). As a result of the implementation of the Protocol on Ireland and Northern Ireland, centralized procedure MAs remain valid for marketing products in Northern Ireland. Pending applications which were submitted to EMA prior to the end of the transition period will either be determined in parallel by the MHRA, or will be put "on hold" until the CHMP issues a positive decision which can be relied upon by MHRA. Converted EU MAs will be treated as if they were granted on the date the corresponding centralized procedure MA was granted and the renewal date will stay the same. If renewals were submitted and no decision was rendered before January 1, 2021, the MHRA will ensure the renewal process is concluded and processed appropriately, and there will be no need to resubmit the application. From January 1, 2021 the requirements for renewal submissions remain the same as required by the EMA and the MAH should continue to submit renewal applications to the MHRA nine months before they expire (or six months in relation to conditional MAs).

Following January 1, 2021, an applicant for a centralized procedure MA must be established in the EU. After this date, companies established in the UK cannot use the centralized procedure and instead must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures (such as the Access Consortium) to obtain a MA to market products in the UK. In addition, for a two-year period from January 1, 2021, MHRA may rely on a decision taken by the European Commission on the approval of a new centralized procedure MA when determining an application for a Great Britain MA; or use the MHRA's decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in Great Britain. Additionally, the 'Unfettered Access Procedure' enables an MAH in Northern Ireland to seek recognition in Great Britain. Post Brexit, the MHRA has been updating various aspects of the regulatory regime for medicines in the UK, including: introducing the Innovative Licensing and Access Procedure to accelerate the time to market and facilitate patient access for innovative medicines; updates to the UK national approval procedure, introducing a 150-day objective for assessing applications for MAs in the UK, Great Britain and Northern Ireland and a rolling review process for MA applications (rather than a consolidated full dossier submission).

UK Orphan Designation

The UK regulatory framework in relation to orphan drug designation is derived from existing EU legislation (as implemented into UK law, through secondary legislation). The European Commission is currently evaluating new legislation in relation to orphan medicines, and after Brexit, these laws will no longer be directly applicable in Great Britain. Since January 1, 2021, there has been no route to obtain pre-MA orphan designation in Great Britain, however, as a result of the implementation of the Protocol on Ireland and Northern Ireland, EU orphan drug designation and time periods of market exclusivity still remain valid for marketing products in Northern Ireland. Instead, the MHRA now reviews applications for Great Britain orphan designation in parallel with the corresponding MA application. The criteria are essentially the same as under the EU regime, but have been tailored for the Great Britain market, i.e. the prevalence of the condition in Great Britain (rather than the EU) must not be more than 5 in 10,000. For medicinal products that have received orphan status on or after January 1, 2021, a period of 10 years orphan market exclusivity is awarded from the date of MA by the MHRA. An additional two years of exclusivity may be added where pediatric data requirements have been met. Products with an orphan designation in the EU may be considered for a Great Britain orphan marketing authorization. However, where centrally authorized MAs have an existing EU orphan designation, these have been converted into Great Britain MAs and shall continue in effect with the remaining period of orphan market exclusivity.

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 in which we are established or in which we run clinical trials, as well as any countries where we may sell, market and distribute any products for which we obtain marketing approval. These laws and regulations cover 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 Regulation (EU) 2016/679 (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 pseudonymized (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.

From January 1, 2021, we are subject to the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, e.g. fines up to the greater of €20 million (£17.5 million) or 4% of the total worldwide annual turnover of the preceding financial year. The relationship between the UK and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how UK data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the UK will be regulated in the long term. These changes may lead to additional costs and increase our overall risk exposure. Currently there is a four to six-month grace period agreed in the TCA, ending June 30, 2021 at the latest, while the parties discuss an adequacy decision. The European Commission published a draft adequacy decision on February 19, 2021. If adopted, the decision will enable data transfers from EU member states to the UK for a four-year period, subject to subsequent extensions.

Recent legal developments in Europe have created complexity and uncertainty regarding transfers of personal data from the EU and the UK to the United States. Most recently, on July 16, 2020, the Court of Justice of the European Union, or CJEU, invalidated the EU-US Privacy Shield Framework, or Privacy Shield, under which personal data could be transferred from the EU to US entities who had self-certified under the Privacy Shield scheme. While the CJEU upheld the adequacy of the standard contractual clauses (a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism, and potential alternative to the Privacy Shield), it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Use of the standard contractual clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals and additional measures and/or contractual provisions may need to be put in place, however, the nature of these additional measures is currently uncertain. The CJEU went on to state that if a competent supervisory authority believes that the standard contractual clauses cannot be complied with in the destination country and the required level of protection cannot be secured by other means, such supervisory authority is under an obligation to suspend or prohibit that transfer.

These recent developments may require us to review and amend the legal mechanisms by which we make and/or receive personal data transfers to or from the U.S. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Employees

As of December 31, 2020, we had 219 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.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of equity-based compensation awards in order to increase shareholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

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 initial public offering (“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, particularly in light of the fast-changing nature of the COVID-19 pandemic, containment measures, vaccine distribution and the related impacts to economic and operating conditions.

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 $58.0 million and $54.8 million for the years ended December 31, 2020 and December 31, 2019, respectively. As of December 31, 2020, we had an accumulated deficit of approximately $261.0 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. Given the length of time typically needed to develop a new drug from the time it enters Phase 1 clinical trials to when it is approved for treating patients, 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, build and expand our intellectual product portfolio, 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, including the planned advancement of AAV-RPGR into the Phase 3 Lumeos clinical trial for the treatment of patients with XLRP and the initiation of a Phase 3 clinical trial of AAV-RPE65 for the treatment of retinal dystrophy associated with mutations in the *RPE65* gene, although we believe that certain of these increases will be partially offset by the research funding in connection with the Collaboration Agreement. 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 have and will continue to increase substantially as a public company and as we continue to add clinical, scientific, operational, financial, manufacturing, compliance and management information systems and personnel, including personnel to support our product development, manufacturing 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"), UK Medicines and Healthcare Regulatory Agency ("MHRA"), 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, as well as continue to expand our manufacturing and supply chain capabilities. This 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. Our ability to raise additional capital when needed may be adversely affected by external factors beyond our control, including changes in the political climate, changes in market interest rates, potential reforms and changes to government negotiation and regulation, the effect of healthcare reform legislation, including those that may limit pricing of pharmaceutical products and drugs, market prices and conditions, prospects for favorable or unfavorable clinical trial results, new product initiatives, the manufacturing and distribution of new products, product safety and efficacy issues, new collaborations, strategic alliances and licensing arrangements, and the COVID-19 outbreak and mitigation measures. 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, 2020, our cash and cash equivalents were $209.5 million. In addition, we expect to receive $38 million in receivables in the first quarter of 2021 from Janssen in connection with the Collaboration Agreement. Based on our cash and cash equivalents at December 31, 2020 and the research funding and milestone payments we expect to receive under the Collaboration Agreement, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the middle of 2023. 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 spend more than expected or consume capital significantly faster than we currently anticipate. 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, including the planned advancement of AAV-RPGR into the Phase 3 Lumeos clinical trial for the treatment of patients with XLRP, 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, including the initiation of a Phase 3 clinical trial of AAV-RPE65 for the treatment of retinal dystrophy associated with mutations in the *RPE65* gene, 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 progress, timing, costs and results of our clinical development program for our product candidate for the treatment of Parkinson's disease, AAV-GAD;

- the development of our product candidate for the treatment of ALS, AAV-UPF1, for our product candidate for the treatment of xerostomia associated with Sjogren's syndrome, AAV-AQP1 and our product candidate for the treatment of neovascular age related macular degeneration, or wet AMD;

- 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, MHRA, 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.

Raising additional capital through the sale of equity or convertible debt securities will dilute your ownership interest, 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 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. 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, MHRA, 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, MHRA, 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 UK or EU until we receive approval for a Marketing Authorization Application, or MAA, from the MHRA or EMA, respectively, and we cannot market them in other countries until we receive any other required regulatory approval in those countries.

Because some of our other product candidates are based on similar technology as our Most Advanced Product Candidates, if any of our 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

The outbreak of the novel coronavirus disease, COVID-19, or other pandemic, epidemic or outbreak of an infectious disease may materially and adversely impact our business, including our preclinical studies and clinical trials.

The COVID-19 pandemic and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce globally, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen.

As a result of the COVID-19 pandemic, we have at times restricted onsite activities, and may continue to restrict onsite activities, to manufacturing functions, laboratory research and certain support activities. We have also experienced some delays in enrolling, treating and monitoring patients in our clinical trials, as well as limited supply chain disruptions. We may experience other disruptions from the COVID-19 pandemic or other pandemic, epidemic or outbreak of an infectious disease that could severely impact our business, preclinical studies, clinical trials and laboratory and manufacturing activities, including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal, state, local or foreign governments, employers and others, or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA, MHRA, EMA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in, the manufacturing of our product candidates due to staffing shortages, governmental restrictions relating to on-site activities, production slowdowns or stoppages and supply chain disruptions;
- slowdowns or problems with the development and startup of our new manufacturing facilities in Shannon, Ireland;
- interruptions in preclinical studies due to restricted or limited operations at our laboratory facilities;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; and
- interruption or delays to our sourced discovery and clinical activities.

The COVID-19 pandemic continues to impact businesses globally and new and more contagious variations of the virus have emerged. The extent to which the outbreak may further impact our business, preclinical studies, clinical trials and laboratory and manufacturing activities will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, the timing, distribution and effectiveness of vaccines, travel restrictions and social distancing in the countries where we do business, business closures or business disruptions, and the effectiveness of actions taken in the countries where we do business to contain and treat the disease, respond to the reduction in global economic activity and resume normal economic and operating conditions. If we or any of the third parties with whom we engage experience prolonged shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted. The pandemic and public and private responses to the pandemic may continue to affect economic conditions and may lead to an economic downturn and/or a recession, at a global scale, which could materially affect our performance, financial condition, results of operations, and cash flows, as well as our ability to raise additional capital.

In addition, we expect the COVID-19 pandemic will continue to affect our employees, our vendors and their employees or the employees of companies with which we do business, which may ultimately disrupt our business operations. We have and will continue to adhere to applicable guidelines and safety measures including work-from-home policies and restricting onsite activities to manufacturing functions, laboratory research and certain support activities as necessary. Employees who are working in our offices are required to quarantine if they are diagnosed with, show symptoms of, or are exposed to someone with, the coronavirus. We may also have to reinstitute a broader work-from-home policy for an undetermined amount of time if COVID-19 cases increase in the jurisdictions where we have offices. An extended period of remote working, whether by our employees, our vendors and their employees or the employees of companies with which we do business may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. In addition, this could increase our cyber security risk due to increases in malware campaigns and phishing attacks preying on the uncertainties surrounding COVID-19, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with regulators, laboratory and manufacturing sites, research or clinical trial sites and other important agencies and contractors.

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 gene therapies have been approved in the United States or in Europe.

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.

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, prior 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. 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 FDA, MHRA and EMA. 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, which could impact the timing and cost of any regulatory approval. 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 ATMPs. ATMPs 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 EU, 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.

Post Brexit, MAAs for ATMPs in Great Britain are regulated nationally and assessed in accordance with the general provisions in place for the licensing of medicines, taking the specific requirements for this group of medicines into account. In Northern Ireland, ATMPs will continue to be authorized according to the EMA's centralized marketing authorization procedure. Definitions for individual classes of ATMPs remain unchanged and classification of ATMPs are undertaken by the MHRA in accordance with EU legislation and current guidance from CAT. Data, traceability, exemptions from licensing, packaging and post-authorization requirements remain in line with EU requirements transposed into UK law. However, if the EMA issues new guidance on ATMPs going forward, there is a risk of regulatory divergence with the MHRA and separate procedures and standards with which we may need to comply.

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, MHRA, 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, MHRA, 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, MHRA, 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, MHRA, 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, MHRA, 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, MHRA, EMA or other regulatory authorities for support of a marketing authorization 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 are currently conducting several ongoing clinical development programs, 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, MHRA, 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 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 COVID-19 pandemic, or natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability; 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, MHRA, 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, MHRA, 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, MHRA, EMA or other regulatory authorities on our clinical development program, and the FDA, MHRA, 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 UK, the EU 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 or the halting of clinical trials, 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. In January 2021, AAV-CNGA3 was designated a Fast Track program by the FDA for the treatment of achromatopsia caused by *CNGA3* mutations.

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. In February 2020, AAV-RPGR for the treatment of X-linked retinitis pigmentosa owing to defects in RPGR was admitted to the PRIME scheme of the EMA.

A sponsor may also seek an RMAT for its product candidates. In 2017, the FDA established the RMAT designation as part of its implementation of the 21st Century Cures Act. A biological product is eligible for RMAT designation if it qualifies as an 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. In a February 2019 final guidance, the FDA also stated that certain gene therapies that lead to a sustained effect on cells or tissues may meet the definition of a regenerative medicine therapy. 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.

Such regulatory designations are within the discretion of the FDA, MHRA, 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, MHRA, 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, AAV-RDH12 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 EU, 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 EU. 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 EU 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 EU, 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 EU, a marketing authorization for an orphan designated product will not be granted if a similar drug has been approved in the EU 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.

Products with an orphan designation in the EU may be considered for a Great Britain orphan marketing authorization. However, where centrally authorized MAs have an existing EU orphan designation, these have been converted into Great Britain MAs and shall continue in effect with the remaining period of orphan market exclusivity. Since the end of the Brexit transition period, there has been no route to obtain pre-MA orphan designation in Great Britain, however, as a result of the implementation of the Protocol on Ireland and Northern Ireland, EU orphan drug designation and time periods of market exclusivity still remain valid for marketing products in Northern Ireland. Instead, the MHRA now reviews applications for Great Britain orphan designation in parallel with the corresponding MA application. Market exclusivity periods between those approved by the MHRA may vary to products which already have an EU orphan designation.

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, for AAV-AIPL1 for the treatment of inherited retinal dystrophy due to defects in *AIPL1* gene and for AAV-RDH12 for the treatment of retinol dehydrogenase 12 (RDH12) mutation-associated retinal dystrophy, 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 EU and Great Britain, the EMA or MHRA, respectively, 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 manufacturers for plasmid are subject to significant regulation with respect to manufacturing our products. Our manufacturing facilities and the third-party manufacturing facilities 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 we completed the acquisition of our second cGMP viral vector manufacturing facility and our first cGMP plasmid and DNA production facility in Shannon, Ireland in January 2021 to expand our manufacturing and supply chain capabilities. However, if we experience slowdowns or problems with our completed facility or the development and startup 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 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, EMA or other regulatory approval of the products will not be granted.

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, MHRA, EMA or other regulatory authorities 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 has and will continue to 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. In January 2021, we completed the acquisition of our second cGMP viral vector manufacturing facility and our first cGMP plasmid and DNA production facility in Shannon, Ireland. Expanding our manufacturing capacity to produce the preclinical, clinical and commercial supply of our products and their components will require completing the development and startup of our new facilities in Ireland, substantial additional expenditures, time, and various regulatory approvals and permits, all of which may be impacted by the COVID-19 pandemic. Further, we will need to hire and train significant numbers of employees and managerial personnel to staff our expanding manufacturing and supply chain operations, including in our new facilities in Ireland. 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. 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 potential commercial demand for our product candidates. 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. This 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. 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 or side effects that may arise in development;
- 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;
- the risk that patients enrolled in clinical trials will drop out of the trials before completion; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or widespread health emergencies, such as the COVID-19 pandemic, or natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability.

In addition, 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 (such as Luxturna marketed by Spark Therapeutics, Inc. for the treatment of RPE65-associated retinal disease) may reduce the number and type of patients available to us.

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. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval, which could negatively impact our business, financial condition, results of operations and prospects.

The regulatory approval processes of the FDA, MHRA, 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, MHRA, 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, the UK or the EU until we receive regulatory approval of a BLA from the FDA or an MAA from the MHRA or EMA, respectively. It is possible that the FDA may refuse to accept for substantive review any BLAs, or the MHRA or 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 UK, the EU or elsewhere, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA, MHRA, 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, MHRA, EMA or other regulatory authorities. The FDA, MHRA 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, MHRA 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, MHRA, 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 Agreement partner obtain FDA, MHRA or EMA approval for AAV-GAD, AAV-RPGR, AAV-CNGB3, AAV-CNGA3, AAV-RPE65 or AAV-AQP1 in the United States or EU, 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, the MHRA in the UK or the EMA in the EU 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, MHRA, 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, MHRA 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, MHRA 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.

Changes in funding for, or disruptions caused by global health concerns impacting, the FDA and other government or regulatory agencies could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed, approved or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other government or regulatory agencies may also slow the time necessary for new product candidates to be reviewed and/or approved, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products and subsequently, on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting business as usual or conducting inspections, reviews or other regulatory activities, it could significantly impact the ability of such regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

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 UK, the EU 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, included 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. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case. The Supreme Court heard the case in November 2020, with a decision expected by June 2021. 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 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, 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 likelihood of implementation of any of these reform initiatives is uncertain, particularly in light of the Biden administration taking office in January 2021. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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

In addition, FDA regulations and guidance may be revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. For example, the results of the 2020 presidential election may impact our business and industry. The Trump administration took several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict whether or how these requirements will be interpreted and implemented, or whether they will be rescinded and replaced under the Biden administration. The policies and priorities of an incoming administration are unknown and could materially impact the regulations governing our product candidates. Any new regulations or guidance, or revisions or reinterpretations of existing regulations or guidance, may impose additional costs or lengthen FDA review times for our product candidates. We cannot determine how changes in regulations, statutes, policies, or interpretations when and if issued, enacted or adopted, may affect our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recalls, replacements, or discontinuance of one or more of our products; and

- additional recordkeeping.

Such changes would likely require substantial time and impose significant costs, or could reduce the potential commercial value of our product candidates, and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any other products would harm our business, financial condition, and results of operations.

In the UK and EU, 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 UK or 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 UK and the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national 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 the UK and 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 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, the UK and the EU, 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 UK the EU 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 UK, EU 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.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention and security of personal information, including HIPAA, the EU's General Data Protection Regulation, or GDPR, and UK data privacy law.

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, receive, 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. 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.

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, the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020, 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 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. Further, the California Privacy Rights Act, or the CPRA, recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. The CCPA, the CPRA or other domestic privacy and data protection laws and regulations may increase our compliance costs and potential liability.

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.

From January 1, 2021, we are subject to the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, e.g. fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. The relationship between the UK and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how UK data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the UK will be regulated in the long term. These changes will lead to additional costs and increase our overall risk exposure. Currently there is a four to six-month grace period agreed in the EU and UK Trade and Cooperation Agreement, ending June 30, 2021 at the latest, whilst the parties discuss an adequacy decision. The European Commission published a draft adequacy decision on February 19, 2021. If adopted, the decision will enable data transfers from EU member states to the UK for a four-year period, subject to subsequent extensions.

Recent legal developments in Europe have created complexity and uncertainty regarding transfers of personal data from the EEA and the UK to the U.S. Most recently, on July 16, 2020, the CJEU invalidated the EU-US Privacy Shield Framework, or Privacy Shield, under which personal data could be transferred from the EEA to US entities who had self-certified under the Privacy Shield scheme. While the CJEU upheld the adequacy of the standard contractual clauses (a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism, and potential alternative to the Privacy Shield), it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Use of the standard contractual clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals and additional measures and/or contractual provisions may need to be put in place, however, the nature of these additional measures is currently uncertain. The CJEU went on to state that if a competent supervisory authority believes that the standard contractual clauses cannot be complied with in the destination country and the required level of protection cannot be secured by other means, such supervisory authority is under an obligation to suspend or prohibit that transfer.

These recent developments may require us to review and amend the legal mechanisms by which we make and/or receive personal data transfers to or from the U.S. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

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 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. In 2017, the FDA 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, Biogen, Inc. and 4D Molecular Therapeutics, Inc. There are a number of companies developing gene therapy products for neurodegenerative diseases, including Voyager Therapeutics, Inc., Brain Neurotherapy Bio, 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. 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, limiting demand or the price we are able to charge, or that could render any products that we may develop obsolete or non-competitive. Our competitors also may obtain FDA, MHRA, 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. 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 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 if approved. Assuming there is such coverage 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 UK, the EU 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.

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 product candidates for sale at competitive prices;
- the convenience and ease of administration;
- 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, and publicity concerning our products or competing products and treatments;
- 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, MHRA, 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 Agreement with them. 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 such capabilities could delay any product launch, which would adversely impact the commercialization of our product candidates. Additionally, if any commercial launch 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 or our collaborators are unable to establish or maintain adequate sales, marketing and distribution capabilities, 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, the UK or the EU, 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, the UK and the EU, such as under our Collaboration 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;
- tighter restrictions on privacy and the collection and use of patient data;
- reduced or loss of 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 COVID-19 pandemic, 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;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- workforce uncertainty in countries where labor unrest is more common than in the United States and compliance with tax, employment, immigration and labor laws for employees living or traveling 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 facilities are 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 we completed the acquisition of our second cGMP viral vector manufacturing facility and our first cGMP plasmid and DNA production facility in Shannon, Ireland in January 2021 to expand our manufacturing and supply chain capabilities. However, if our current facility is damaged, suffers any form of delay or regulatory challenges, we experience slowdowns or problems with the development and startup 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. While we expect to begin our own plasmid manufacturing capabilities in our Shannon, Ireland facilities during 2021, 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 COVID-19 pandemic , 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, including failure to provide appropriate quantities in a timely manner;
- 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 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.

We have relied, and we expect to continue to rely, on third parties to conduct, supervise and monitor our preclinical studies and clinical trials, and if these third parties perform in an unsatisfactory manner, our business could be harmed.

We expect to rely on CROs, clinical trial sites, and other vendors to ensure our preclinical studies and clinical trials are conducted properly and on time. We may also engage third parties such as clinical data management organizations, medical institutions and clinical investigators to conduct or assist in our clinical trials or other preclinical and clinical research and development work. While we will have agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our third-party service providers' activities. Nevertheless, we will be responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal, quality, regulatory and scientific standards. Our reliance on these third parties does not relieve us of our regulatory responsibilities. For example, we expect to conduct the Phase 3 Lumeos clinical trial of AAV-RPGR for the treatment of patients with XLRP caused by mutations in the *RPGR* gene at multiple clinical trial sites in North America and Europe. If any locations terminate the clinical trial, we would be required to find another party to conduct any new trials. We may be unable to find a new party to conduct new trials of our product candidates or obtain clinical supply of our product candidates or AAV vectors for such trials. If we elect to internalize some or all activities related to the conduct of our preclinical studies or clinical trials that are currently performed by our third-party service providers, or if we are required to do so due to a service provider's termination of our relationship, then we may be required to source additional technology and personnel in order to perform the relevant activities. We may be unsuccessful in our efforts to internalize some or all relevant activities, either on the desired timeline or at all.

Our third-party service providers are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time, attention, expertise and resources to our clinical and nonclinical programs. These third-party service providers may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If our third-party service providers do not successfully carry out their contractual duties or obligations or fail to meet expected deadlines, including as a result of the impact of the COVID-19 pandemic, or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our preclinical studies or clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates could be harmed, our costs could increase, and our ability to generate revenues could be delayed.

If our relationship with any CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have an adverse impact on our business, financial condition and prospects.

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 research institutions, universities and other third parties. We may also 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. If we fail to comply with our obligations to any of our current or future 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.

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 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 might 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. In addition, 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. 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. 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.

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. 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 parties 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. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents, and 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 we are not successful in defending such claims, it 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.

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.

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. 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, the UK, the EU 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 UK, the EU 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 UK, the EU 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.

Obtaining and enforcing patents in the biotechnology and genetic medicine industries involve both technological complexity and legal complexity. 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 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.

In addition, 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 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. 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.

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, the UK or the EU. 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.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States, the UK and the EU, 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, or the efforts of our licensors or collaborators, to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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 UK and the EU, our product candidates may be eligible for term extensions based on similar legislation. In each of these jurisdictions, 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;
- 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; and
- 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.

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. We may also 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. 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.

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, UK 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 or equipment 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, MHRA, 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.

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, 2020, we had 219 full-time employees. We expect to continue to significantly expand our organization, including hiring and training significant numbers of employees and managerial personnel to staff our expanding manufacturing and supply chain operations in our new facilities in Ireland. 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 certain of 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. 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 time, costs and diversion of management resources to defend the related litigation;
- 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) applicable laws and regulations of the FDA, MHRA, EMA and other regulatory or governmental 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 business partners and service providers may be vulnerable to cybersecurity risks.

Our computer systems, as well as those of our business partners and service providers, are vulnerable to damage from computer viruses, unauthorized access, hardware and software failures, natural disasters, 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, process 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. 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 business partners' and service providers' 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.

The UK's withdrawal from the EU has resulted in changes to regulatory requirements and has had and may continue to 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, commonly referred to as "Brexit" and, following the expiry of the Brexit transitional period on December 31, 2020, the UK now operates under a distinct regulatory regime and certain EU laws now only apply to the UK in respect of Northern Ireland (as laid out in the Protocol on Ireland and Northern Ireland, including but not limited to MAs). The MHRA is now the UK's standalone regulator. Although the UK and EU have now reached an agreement on its future trading relationship (to be implemented in the TCA from January 1, 2021), the agreement does not cover all regulatory areas regarding supply of medicinal product, which will likely be subject to future bilateral discussions going forward and could further change the relationship between the UK and the EU in this regard.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". However, new legislation such as the EU Clinical Trials Regulation, ("EU CTR") or in relation to orphan medicines will not be applicable. In addition, as there is no general power to amend the "retained EU law", the UK government has introduced a new Medicines and Medical Devices Bill which seeks to address regulatory gaps through implementing regulations and delegated powers covering, among other things, the fields of human medicines and clinical trials of human medicines. Despite regulatory authorities in the UK indicating in the bill that new UK rules will closely align with EU laws, detailed proposals are yet to be published and there is still a risk of regulatory divergence.

Brexit has created additional administrative burdens that are likely to result in disruptions to and uncertainty surrounding our planned clinical trials and activities in the UK and the EU, which may impact relationships with our existing and prospective customers, partners, vendors and employees. Already, various benefits of membership no longer apply to the UK for clinical trials, such that, for example, UK sponsored trials that span several EU countries now need to have an individual or organization in the EU to act as a legal representative, or sponsor and it is unclear whether the UK will have access to new EU clinical trial databases such as the Clinical Trial Information System going forward, (the centralized EU Portal for clinical trial information storage). Additionally, new rules apply to the import of investigational medicinal products from the EU and EEA to Great Britain.

While agreement on the terms of the TCA has avoided a "no deal" Brexit scenario, and provides in principle for quota and tariff free trading of goods, it is nevertheless expected that the TCA will result in the creation of non-tariff

barriers (such as increased shipping and regulatory costs and complexities) to the trade in goods between the UK and EU. Further, the TCA does not provide for the continued free movement of services between the UK and EU and also grants each of the UK and EU the ability, in certain circumstances, to unilaterally impose tariffs on one another. The TCA does provide for the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued. However, it is important to note that significant regulatory gaps still exist and the TCA does not contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards between the parties, for example, in relation to batch testing and pharmacovigilance, which remain subject to further discussions.

For MAs, an applicant for a centralized procedure MA must be established in the EU. After Brexit, companies established in the UK cannot use the centralized procedure and instead must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures (such as the Access Consortium) to obtain an MA to market products in the UK. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a Great Britain MA; or use the MHRA's decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in Great Britain. Additionally, the 'Unfettered Access Procedure' enables an MAH in Northern Ireland to seek recognition in Great Britain.

The full impact of these new arrangements and requirements, both on our existing processes and our ability to adjust our business and operations to operate successfully in the UK and EU, as well as more broadly on UK-EU cross-border trade and the economy, are expected to become clearer in the course of 2021. In particular, it remains to be seen whether the initial implementation of, and adjustment of UK-EU trading processes for, the TCA could disrupt or otherwise negatively impact our business and operations. These negative impacts could include amongst others a decrease in foreign direct investment in the UK, an increase of our costs, disruption of our supply chains, restrictions on our ability to access capital and depression on economic activity or economic instability, which could in turn lead to a reduction in asset valuations, currency exchange rates and credit ratings.

In addition, the TCA has imposed additional restrictions on the free movement of people between the UK and the EU, which could have a material adverse effect on us, since we compete in these jurisdictions for well qualified employees in all aspects of our business. Any impact on our ability to attract new employees and to retain existing employees in their current jurisdictions could decrease our competitiveness. Any of these factors could have an adverse effect on our business, financial condition, results of operations, and prospects.

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. Additionally, the trading prices for our ordinary shares and the shares of other smaller biopharmaceutical companies have been and continue to be highly volatile as a result of the COVID-19 pandemic. 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 and during the COVID-19 pandemic. 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, as well as general economic,

political and market conditions such as recessions, interest rate changes or international currency fluctuations, 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 significantly influence all matters submitted to shareholders for approval.

As of December 31, 2020, 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 41.1% of our outstanding ordinary shares.

As a result, if these shareholders choose to act together, they would be able to 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 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.

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:

- reduced disclosure obligations relating to the presentation of financial statements in the "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 ordinary 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 ordinary 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, 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 share price may be more volatile.

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.

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

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

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 UK 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, or PFIC, 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 current and anticipated composition of our income, assets and operations, we do not believe we were a PFIC for the taxable year ended on December 31, 2020, 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 ended on December 31, 2020 or 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. The value of our assets generally is determined by reference to the market price of our ordinary shares, which may fluctuate considerably. In addition, the composition of our income and assets is affected by how, and how quickly, we spend any cash we raise. If we were to be classified as a PFIC for any taxable year during which a U.S. holder holds our ordinary shares, certain materially adverse U.S. federal income tax consequences could apply to such U.S. holder.

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 that are subject to change or differing interpretations, including on a retroactive basis. Any such 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.

We have significant U.S. federal and state net operating losses, or NOLs, and UK and Netherlands carryforward tax losses which we may not be able to realize or which may be restricted under applicable law. We also benefit from certain tax incentive regimes, such as research and development tax credits. Any adverse change to these regimes, the application thereof or challenges to the tax position we have adopted under these rules could adversely affect our results of operations and financial condition.

As of December 31, 2020, we had federal and state NOL carryforwards in the United States of $34.7 million and $34.4 million, respectively, cumulative carryforward tax losses in the UK of $142.2 million, and $26.1 million in the Netherlands, which we expect to be available to reduce future taxable income subject to any relevant restrictions (including those in the U.S. and UK that limit the percentage of taxable income that can be reduced by NOLs and carried forward losses). The U.S. federal and state NOLs incurred prior to January 1, 2018 in the amount of approximately $6.8 million and $6.7 million, respectively, will begin to expire in 2035. U.S. federal NOLs generated after December 31, 2017 are not subject to expiration but such NOLs may only offset 80% of taxable income for taxable years beginning after December 31, 2020. As of December 31, 2020, we also had orphan drug and research and development credits in the U.S. in the amount of $4.6 million and research and development credits in the UK of $1.2 million. The UK carryforward tax losses will continue indefinitely, subject to relevant restrictions, under current UK legislation. The Netherlands carryforward tax losses expire after nine years from the date incurred prior to 2019 and six years for tax losses incurred after 2018.

The NOLs and UK and Netherlands carryforward tax losses are subject to review and possible adjustment by the U.S. federal and state and UK tax authorities. Additionally, NOLs and UK carryforward tax losses, and research and development tax credits, may become subject to limitations in the event of certain cumulative changes in the ownership interest of significant shareholders, as determined under Sections 382 of the United States 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, 2019, there were no limitations in the UK. However, for U.S. federal tax purposes, we have determined that ownership changes occurred in August 2016 and June 2018. We are still in the process of determining the annual limitation on NOLs as a

result of such ownership changes. Subsequent ownership changes and changes to the U.S. federal or state or UK tax rules in respect of the utilization of NOLs and carryforward tax losses may further affect the limitation in future years.

General Risk Factors

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

We have, and may in the future, 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.

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 may adversely affect us, particularly between the U.S. dollar on the one hand, and the pound sterling and euro on the other hand. As a result, our business and the market price of our securities may be affected by such fluctuations, 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.

Our management team has broad discretion as to the use of the net proceeds from public and private equity or debt financings and the investment of these proceeds may not yield a favorable return. We may invest the proceeds in ways with which our shareholders disagree.

We have broad discretion in the application of any net proceeds we may receive pursuant to any past or future equity or debt financings. Shareholders may not agree with our decisions, and our use of the proceeds and our existing cash and cash equivalents may not improve our results of operation or enhance the value of our ordinary shares. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the market price of our ordinary shares to decline. In addition, until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value. Additionally, our existing cash and cash equivalents are subject to general credit, liquidity, market and interest rate risks, which have been and may, in the future, be exacerbated by a U.S. and/or global financial crises. We may realize losses in the fair value of certain of our investments or a complete loss of these investments if the credit markets tighten, which would have an adverse effect on our results of operations, liquidity and financial condition.

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.

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, 2020 for additional information.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Our principal office is located at 450 East 29th Street, New York, New York, 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.

In January 2021, we completed the acquisition of a second cGMP viral vector manufacturing facility and a cGMP plasmid and DNA production facility located in Buildings 2 and 3, Block K, Airport Avenue, Shannon Free Zone, Shannon, Ireland. The campus encompasses an aggregate of 150,000 square feet. We also entered into a lease for each property providing for a long leasehold interest of approximately 191 years.

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 Select Market under the symbol "MGTX." Prior to that time, there was no public market for our stock.

Holders of Record

As of March 8, 2021, there were 54 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

None.

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 Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Form 10-K, 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 that was renamed MeiraGTx Netherlands B.V., a biopharmaceutical company developing gene therapy for different indications using viral mediated gene transfer and specializing in the development of viral gene therapy vectors, in particular adeno-associated virus (AAV-) based therapeutics. In April 2020, we acquired Emrys Bio Inc., a Delaware corporation that was renamed MeiraGTx Bio Inc., a pre-clinical biopharmaceutical company developing brain-derived neurotrophic factor gene therapy for treatment of genetic obesity disorders, as well as the development of gene therapy product candidates for other central nervous system diseases. 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, 2020, we received gross proceeds of approximately $446.0 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 Agreement"). As of December 31, 2020, we had cash and cash equivalents of $209.5 million, as well as $38.5 million in receivables due from Janssen in the first quarter of 2021 in connection with the Collaboration Agreement.

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, 2020 and 2019 were $58.0 million and $54.8 million, respectively. As of December 31, 2020, we had an accumulated deficit of $261.0 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 Agreement. Additionally, pursuant to the Collaboration Agreement, we are eligible to receive research and development funding and potential milestone payments and royalties.

Our total operating expenses were $78.1 million and $71.6 million for the years ended December 31, 2020 and 2019, respectively. While we expect our operating expenses to increase substantially in connection with our ongoing development activities related to our product candidates, including the planned advancement of AAV-RPGR into the Phase 3 Lumeos clinical trial for the treatment of patients with XLRP and the initiation of a Phase 3 clinical trial of AAV-RPE65 for the treatment of retinal dystrophy associated with mutations in the *RPE65* gene, we believe that certain of these increases will be partially offset by the research funding in connection with the Collaboration Agreement. In addition to these planned Phase 3 trials, we anticipate that our expenses will also increase due to costs associated with our clinical development program targeting achromatopsia due to mutations in the *CNGB3* or *CNGA3* gene. 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 expect to file an IND application for AAV-GAD in the third quarter of 2021 following the release of the clinical material manufactured in our

London cGMP facility. We also incurred expenses during the year ended December 31, 2020 and expect to continue 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 and the acquisition, development and startup of our new Shannon, Ireland manufacturing facilities, we raised net proceeds of $81.9 million during the year ended December 31, 2020 from an at-the market offering and a public offering of our ordinary shares. We will require additional capital in the future, 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, 2020 and the research funding and milestone payments we expect to receive under the Collaboration Agreement, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the middle of 2023. 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.

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 and Anticipated 2021 Milestones

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

- We reported preliminary data from the Phase 1 AQUAx clinical trial in December 2020.
  - Of the three patients treated in Cohort 1, one patient reached the 12-month assessment and two passed the six-month assessment. In all patients, the investigational gene therapy AAV-hAQP1 has been well tolerated with no dose limiting toxicity and no serious adverse events reported.
  - Encouraging responses have been seen in patient-reported measures of xerostomia symptoms and in salivary output in the patients treated in Cohort 1.
  - Complete resolution of symptoms was observed in the patient who has reached the 12-month timepoint.
- We continue to activate clinical trial sites in our Phase 1 AQUAx study, with two sites re-opened after shutdowns due to COVID-19, and all five sites are anticipated to be open and enrolling patients in the first half of 2021.
- The single center Phase 1 dose-finding study of AAV-AQP1 at the National Institutes of Health (NIH) also continues to enroll patients. Enrollment in the fourth dose escalation cohort is now ongoing.

AAV-RPGR for the Treatment of X-Linked Retinitis Pigmentosa (XLRP):

- We and our development partner Janssen are preparing to initiate the Phase 3 Lumeos clinical trial.
- In 2020, we and Janssen were granted Priority Medicines (PRIME) and Advanced Therapy Medicinal Product (ATMP) designations for AAV-RPGR.
- In 2020, we and Janssen announced positive 6-, 9- and 12-month data from the Phase 1/2 clinical study (MGT009) of AAV-RPGR at the American Society of Retina Specialists (ASRS) Annual Meeting, the European Society of Retina Specialists (EURETINA), and the American Academy of Ophthalmology Annual Meeting:
  - Data from each time point demonstrated that patients treated with low and intermediate dose AAV-RPGR experienced statistically significant improvement in retinal sensitivity. Nine-month data also indicated significant improvement in vision-guided mobility. At 12-months, six of seven patients continued to show improved or stable vision in the treated eye.

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

- We anticipate filing an Investigational New Drug application (IND) by the third quarter of 2021, with material that has been manufactured with our in-house proprietary manufacturing process at our cGMP manufacturing facility in London.

AAV-RPE65 for the Treatment of *RPE65*-associated Retinal Dystrophy:

- We anticipate initiating a Phase 3 pivotal trial of AAV-RPE65 in the second half of 2021.

AAV-CNGB3 and AAV-CNGA3 for the Treatment of Achromatopsia (ACHM):

- We and Janssen continue to advance our ongoing clinical development of AAV-CNGB3 and AAV-CNGA3 for the treatment of ACHM associated with mutations in the *CNGB3* and *CNGA3* genes.
  - On January 26, 2021 the U.S. Food and Drug Administration (FDA) granted Fast Track designation to our AAV-CNGA3 gene therapy product candidate for the treatment of ACHM caused by mutations in the *CNGA3* gene.
  - We and Janssen have now completed dosing of both adults and pediatric patients in the Phase 1/2 dose escalation study of AAV-CNGA3 and expect to provide an update on further clinical studies for both AAV-CNGB3 and AAV-CNGA3 later in 2021.

Riboswitch Gene Regulation Platform:

- We expect to present *in-vivo* data from our proprietary riboswitch gene regulation platform in the second half of 2021, demonstrating regulation of multiple therapeutic genes in multiple tissues.

Recent Corporate Development Highlights

Second Viral Vector Manufacturing Facility and Plasmid and DNA Production Facility

- We expanded our industry-leading manufacturing capabilities by acquiring and building a second wholly owned cGMP viral vector manufacturing facility as well as a cGMP plasmid and DNA production facility located in Shannon, Ireland.
- The campus encompasses approximately 150,000 square feet serving numerous functions: high capacity cGMP manufacturing hub, clinical supply storage, QC laboratories for global release, up to ten flexible and scalable viral vector suites, fully scalable automated fill and finish, an extensive warehouse and a separate internal cGMP plasmid and DNA manufacturing facility.
- Construction of the cGMP plasmid and DNA manufacturing facility has been completed, with the cGMP viral vector manufacturing facility expected to be completed by the end of 2021.

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

- We continue to increase the number of personnel across key functional areas to support our broad pipeline of optimized investigational gene therapies. Our team now includes more than 215 full-time 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 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 facilities.

We expense research and development costs as incurred.

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, including the planned advancement of AAV-RPGR into the Phase 3 Lumeos clinical trial for the treatment of patients with XLRP and the initiation of a Phase 3 clinical trial of AAV-RPE65 for the treatment of retinal dystrophy associated with mutations in the *RPE65* gene, and continue to discover and develop additional product candidates. Certain of these increases in research and development costs will be partially offset by the research funding provided in connection with the Collaboration 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, MeiraGTx Ireland DAC, MeiraGTx Netherlands B.V. and MeiraGTx B.V. are measured using the foreign subsidiaries' local currency as the functional currency. These entities' cash accounts holding U.S. dollars and intercompany payables and receivables 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.

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 GAAP. 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, 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.

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 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 transfer 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 years ended December 31, 2020 and 2019.

As of December 31, 2020, we had federal and state net operating losses (“NOLs”) in the United States of approximately $34.7 million and $34.4 million, respectively, and carryforward tax losses in the UK of approximately $142.2 million and in the Netherlands of approximately $26.1 million, which are available to reduce future taxable income. The U.S. federal and state NOLs 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. NOLs incurred after December 31, 2017 and the UK carryforward tax losses will be indefinitely carried forward. The Netherlands carryforward tax losses expire after nine years from the date incurred prior to 2019 and six years for tax losses incurred after 2018. As of December 31, 2020, we also had orphan drug and research and development credits in the U.S. in the amount of $5.1 million, which

will begin to expire 2036 and research and development credits in the UK in the amount of $1.2 million, which can be carried forward indefinitely.

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.

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.

Restricted Share Units

The Company grants restricted share units ("RSUs") to employees and non-employee consultants as compensation for services performed. Awards of RSUs 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 RSUs, 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 RSUs is determined using the closing market price of the Company's ordinary shares on the date of grant.

Restricted Shares

In connection with certain employment, service 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

Comparison of the Years Ended December 31, 2020 and 2019

	2020	2019	Change
License revenue - related party	$ 15,562,985	$ 13,291,956	$ 2,271,029
Operating expenses:			
General and administrative	44,206,921	46,684,297	(2,477,376)
Research and development	33,910,481	24,875,659	9,034,822
Total operating expenses	78,117,402	71,559,956	6,557,446
Loss from operations	(62,554,417)	(58,268,000)	(4,286,417)
Other non-operating income (expense)			
Foreign currency gain	3,426,152	3,199,774	226,378
Interest income	1,275,464	370,603	904,861
Interest expense	(139,203)	(48,612)	(90,591)
Net loss	(57,992,004)	(54,746,235)	(3,245,769)
Other comprehensive income:			
Foreign currency translation for the years ended December 31, 2020 and 2019, respectively	(3,102,864)	(2,087,708)	(1,015,156)
Total comprehensive loss	$ (61,094,868)	$ (56,833,943)	$ (4,260,925)

License Revenue

License revenue was $15.6 million for the year ended December 31, 2020, compared to $13.3 million for the year ended December 31, 2019. This increase represents the increased amortization of the $100.0 million upfront payment received in connection with the Collaboration Agreement.

General and Administrative Expenses

General and administrative expenses were $44.2 million for the year ended December 31, 2020, compared to $46.7 million for the year ended December 31, 2019. The decrease of $2.5 million was primarily due to a decrease in payroll and payroll related costs of $6.9 million and travel expenses of $1.0 million, which was partially offset by increases in insurance of $2.3 million, share-based compensation of $1.5 million, rent of $1.1 million, professional fees of $0.2 million and $0.3 in other general and administrative expenses.

Research and Development Expenses

Research and development expenses for the years ended December 31, 2020 and 2019 were as follows (in millions):

	2020	2019	Change
Gross research and development expenses	$ 96.6	$ 65.0	$ 31.6
Janssen reimbursements	(57.4)	(28.1)	(29.3)
Tax incentive reimbursement	(5.3)	(12.0)	6.7
Research and development expenses	$ 33.9	$ 24.9	$ 9.0

Gross research and development expenses for the year ended December 31, 2020 increased $31.6 million as compared to the prior year primarily due to an increase in manufacturing of our clinical trial materials of $12.2 million, payroll and payroll related costs of $8.3 million, acquired research and development of $7.7 million, depreciation of $1.4 million, rent and facility costs of $1.2 million and share-based compensation of $1.0 million, which was partially offset by a decrease in research and clinical trial costs related to our ophthalmology and salivary gland programs of $1.2 million.

Reimbursements under the Collaboration Agreement for the year ended December 31, 2020 increased $29.3 million as compared to the prior year primarily due to an increase in activity in the programs licensed under the Collaboration Agreement.

Tax incentive reimbursement for the year ended December 31, 2020 decreased $6.7 million as compared to the prior year primarily due to the 2018 and 2019 UK refundable research and development credit being recorded in 2019. In 2020, only the 2020 UK refundable research and development credit was recorded.

Foreign Currency Gain

Foreign currency gain was $3.4 million for the year ended December 31, 2020 compared to a gain of $3.2 million for the year ended December 31, 2019. The change of $0.2 million was primarily due to a strengthening of the pound sterling and euro against the U.S. dollar in 2020.

Interest Income

Interest income was $1.3 million for the year ended December 31, 2020 compared to $0.4 million for the year ended December 31, 2019. The increase was due to a higher average cash balance during 2020 and a reallocation of funds into an account earning a higher interest rate.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. For the year ended December 31, 2020, we used $64.0 million in cash flows from operations. We did not generate positive cash flows from operations during the year 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, on August 4, 2020 we entered into agreements to acquire our

second cGMP viral vector manufacturing facility and our first cGMP plasmid and DNA production facility in Shannon, Ireland to expand our manufacturing and supply chain capabilities. We closed on the acquisition of the first building in August 2020 and closed on the second building in January 2021. As a result of these incurred and expected expenses, we raised additional funds during the year ended December 31, 2020 as further described below, and will need to raise additional capital in the future 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 Agreement, which also provides us with research funding, and we are eligible to receive potential milestone payments and royalties.

Based on our current cash and cash equivalents at December 31, 2020 and the research funding and milestone payments we expect to receive under the Collaboration Agreement, we estimate that we will be able to fund our operating expenses and capital expenditure requirements into the middle of 2023. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

Cash Flows

We had $209.5 million and $227.4 million of cash, cash equivalents and restricted cash as of December 31, 2020 and 2019, respectively.

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

	For the years ended December 31,	
	2020	2019
Net cash (used in) provided by operating activities	$ (63,967,799)	$ 20,044,897
Net cash used in investing activities	(37,020,433)	(9,370,081)
Net cash provided by financing activities	82,727,383	148,234,904
(Decrease) increase in cash	$ (18,260,849)	$ 158,909,720

Operating Activities

During the year ended December 31, 2020, our cash used in operating activities of $64.0 million was primarily due to our net loss of $58.0 million as we incurred expenses associated with research activities on our clinical programs, manufacturing of our clinical trial materials, preclinical research programs and general and administrative expenses. The net loss included non-cash charges of $26.7 million, which consisted of $7.7 million for acquired research and development, $18.4 million of share-based compensation, $3.4 million of a foreign currency gain and $4.1 million of depreciation and amortization. Additionally, operating assets, consisting of accounts receivable-related party, prepaid expenses, tax incentive receivable, security deposits and other current assets, increased by $20.8 million and operating liabilities, consisting of accounts payable, accrued expenses, and deferred revenue-related party, decreased by $11.9 million.

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 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.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2020 of $37.0 million consisted primarily of $14.0 million in payments for the acquisition of the first building and long-term lease for our manufacturing facilities in Ireland, $2.1 million for the purchase of an intangible asset and $20.9 million for purchases of property and equipment for our manufacturing, laboratory and process development facilities and buildout costs of our facilities in the UK and Ireland.

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

Financing Activities

Net cash provided by financing activities was $82.7 million for the year ended December 31, 2020, which consisted primarily of gross proceeds of $87.0 million from an at-the market offering and a public offering of our ordinary shares, which was offset by $5.1 million in offering costs, as well as $0.8 million from the exercise of share options.

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.

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, the United Kingdom, Ireland and the Netherlands. 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, 2020, 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 $209.5 million as of December 31, 2020, 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, 2020. We had cash, cash equivalents and restricted cash of $227.4 million as of December 31, 2019, 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, 2020 AND 2019
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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, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, shareholders' equity and cash flows for each of the two years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

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, 2021

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED BALANCE SHEETS

	December 31, 2020	December 31, 2019
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 209,520,355	$ 227,233,384
Accounts receivable - related party	38,479,371	23,337,377
Prepaid expenses	7,081,747	4,464,085
Tax incentive receivable	12,930,062	11,974,437
Other current assets	4,564,441	1,970,585
Total Current Assets	272,575,976	268,979,868
Property and equipment, net	44,041,903	23,858,108
Intangible assets, net	2,119,011	—
In-process research and development	852,085	777,655
Security deposits	812,344	951,138
Restricted cash	—	123,376
Other assets	213,722	195,053
Right-of-use assets	43,082,359	29,002,448
TOTAL ASSETS	$ 363,697,400	$ 323,887,646
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 7,134,204	$ 3,759,339
Accrued expenses	20,860,820	18,083,757
Lease obligations, current	2,582,999	1,674,210
Deferred revenue - related party, current	23,544,583	25,678,515
Other current liabilities	24,453	—
Total Current Liabilities	54,147,059	49,195,821
Deferred revenue - related party	49,297,194	60,535,576
Lease obligations	19,665,841	21,504,340
Asset retirement obligations	1,814,338	1,654,755
Deferred income tax liability	213,722	195,053
TOTAL LIABILITIES	125,138,154	133,085,545
COMMITMENTS		
SHAREHOLDERS' EQUITY:		
Ordinary Shares, $0.00003881 par value, 1,288,327,750 authorized, 44,189,150 and 36,791,906 shares issued and outstanding at December 31, 2020 and 2019, respectively	1,716	1,429
Capital in excess of par value	504,482,392	395,630,666
Accumulated other comprehensive loss	(4,896,906)	(1,794,042)
Accumulated deficit	(261,027,956)	(203,035,952)
Total Shareholders' Equity	238,559,246	190,802,101
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	$ 363,697,400	$ 323,887,646

See Notes to Consolidated Financial Statements

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

	For the Year Ended December 31,	
	2020	2019
License revenue - related party	$ 15,562,985	$ 13,291,956
Operating expenses:		
General and administrative	44,206,921	46,684,297
Research and development	33,910,481	24,875,659
Total operating expenses	78,117,402	71,559,956
Loss from operations	(62,554,417)	(58,268,000)
Other non-operating income (expense):		
Foreign currency gain	3,426,152	3,199,774
Interest income	1,275,464	370,603
Interest expense	(139,203)	(48,612)
Net loss	(57,992,004)	(54,746,235)
Other comprehensive loss:		
Foreign currency translation	(3,102,864)	(2,087,708)
Total comprehensive loss	$ (61,094,868)	$ (56,833,943)
Net loss	$ (57,992,004)	$ (54,746,235)
Basic and diluted net loss per ordinary share	$ (1.54)	$ (1.65)
Weighted-average number of ordinary shares outstanding	37,724,189	33,161,860

See Notes to Consolidated Financial Statements

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
FOR THE YEARS ENDED DECEMBER 31, 2020 AND 2019

	Ordinary Shares	Amount	Capital in Excess of Par Value	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Equity
Balance at January 1, 2019	27,386,632	$ 1,064	$ 229,054,460	$ 293,666	$ (148,289,717)	$ 81,059,473
Issuance of shares in connection with a license agreement	158,832	6	1,966,334	—	—	1,966,340
Issuance of 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 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
Issuance of shares in connection with asset acquisition	544,500	21	7,684,980	—	—	7,685,001
Issuance of shares in at-the-market offering, net of issuance costs of $505,650	993,448	39	12,657,497	—	—	12,657,536
Issuance of shares in connection with public placement, net of issuance costs of $4,635,362	5,750,000	223	69,251,915	—	—	69,252,138
Exercise of share options	109,296	4	840,754	—	—	840,758
Share-based compensation	—	—	18,416,580	—	—	18,416,580
Foreign currency translation	—	—	—	(3,102,864)	—	(3,102,864)
Net loss for the year ended December 31, 2020	—	—	—	—	(57,992,004)	(57,992,004)
Balance at December 31, 2020	44,189,150	$ 1,716	$ 504,482,392	$ (4,896,906)	$ (261,027,956)	$ 238,559,246

See Notes to Consolidated Financial Statements

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS

	For the Year Ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (57,992,004)	$ (54,746,235)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Ordinary shares issued in connection with license agreement	—	1,966,334
Share-based compensation expense	18,416,580	15,928,970
Foreign currency gain	(3,426,152)	(3,199,774)
Depreciation and amortization	4,171,626	2,238,560
Net change in right-of-use assets and liabilities	(387,180)	1,107,805
Loss on disposal of equipment, furniture and fixtures	212,994	—
Gain on termination of lease liability	(143,590)	—
Amortization of interest on asset retirement obligations	136,069	20,621
Issuance of shares in connection with asset acquisition	7,685,001	—
(Increase) decrease in operating assets:		
Accounts receivable - related party	(15,401,913)	(23,886,573)
Prepaid expenses	(2,366,269)	(2,259,984)
Tax incentive receivable	(714,672)	(8,401,283)
Other current assets	(2,520,087)	(178,805)
Security deposits	164,183	(796,753)
Increase (decrease) in operating liabilities:		
Accounts payable	1,565,763	(8,681)
Accrued expenses	2,171,273	6,518,766
Other current liabilities	23,564	—
Deferred revenue - related party	(15,562,985)	85,741,929
Net cash (used in) provided by operating activities	(63,967,799)	20,044,897
Cash flows from investing activities:		
Purchase of property and equipment	(20,923,556)	(8,980,425)
Payment for right of use asset	(13,968,492)	—
Purchase of intangible asset	(2,128,385)	—
Purchase of Arthrogen, net of acquired cash	—	(389,656)
Net cash used in investing activities	(37,020,433)	(9,370,081)
Cash flows from financing activities:		
Payments on lease obligations - financing leases	(23,049)	(24,857)
Exercise of share options	840,758	557,606
Proceeds from the issuance of ordinary shares	87,050,686	155,200,007
Issuance costs in connection with ordinary shares	(5,141,012)	(7,497,852)
Net cash provided by financing activities	82,727,383	148,234,904
Net (decrease) increase in cash, cash equivalents and restricted cash	(18,260,849)	158,909,720
Effect of exchange rate changes on cash	424,444	243,489
Cash, cash equivalents and restricted cash at beginning of year	227,356,760	68,203,551
Cash, cash equivalents and restricted cash at end of year	$ 209,520,355	$ 227,356,760
Supplemental disclosure of non-cash transactions:		
Issuance of shares in connection with asset acquisition	$ 7,685,001	$ —
Issuance of shares in connection with a license agreement	$ —	$ 1,966,334
Fixed asset acquisition included in accounts payable and accrued expenses at end of period	$ 1,615,127	$ 1,519,454
Issuance of shares in connection with payables	$ —	$ 421,500
Right-of-use assets obtained in exchange for lease liabilities	$ 1,889,065	$ 23,324,609
Reclassification of property and equipment to right-of-use asset	$ —	$ 7,409,789
Asset retirement obligations in connection with a lease	$ —	$ 1,501,290
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 3,134	$ 1,462

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: ocular diseases, including inherited retinal diseases as well as large degenerative 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. Additionally, on August 4, 2020, the Company entered into agreements to acquire its second cGMP viral vector manufacturing facility and its first cGMP plasmid and DNA production facility in Shannon, Ireland to expand its manufacturing and supply chain capabilities. The Company closed on the acquisition of the first building in August 2020 and closed on the acquisition of the second building in January 2021.

Acquisitions

On April 9, 2020, the Company acquired Emrys Bio Inc. ("Emrys"), a pre-clinical biopharmaceutical company developing brain-derived neurotrophic factor gene therapy for treatment of genetic obesity disorders, as well as the development of gene therapy product candidates for other central nervous system diseases. Emrys was renamed MeiraGTx Bio, Inc.

On October 17, 2019, the Company acquired 100% of the outstanding equity of Arthrogen B.V. ("Arthrogen"), 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. Arthrogen was renamed MeiraGTx Netherlands B.V.

These acquisitions are 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, 2020 totaled $261,027,956, 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; expanding and protecting the Company's intellectual property portfolio; dependence on third parties; dependence on key personnel; the COVID-19 pandemic and mitigation measures. For the year ended December 31, 2020, the Company used $63,967,799 in cash flows from operations and there are no assurances that the Company will generate positive cash flows in the future. Additionally, 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, 2020, the Company had cash and cash equivalents in the amount of $209,520,355, 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 also receives 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 and cash equivalents on hand at December 31, 2020 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.

There are also many uncertainties regarding the pandemic caused by the novel coronavirus, or COVID-19, and the Company continues to monitor the impact of the pandemic on all aspects of its business, including how the pandemic will impact its financial condition, liquidity, operations, clinical studies, employees, vendors, and industry. While the pandemic did not materially affect the Company's financial results and business operations in the year ended December 31, 2020, the Company is unable to predict the impact that COVID-19 will have on its financial position and operating results in future periods due to numerous uncertainties. The Company will continue to assess the evolving impact of the COVID-19 pandemic and will make adjustments to its operations as necessary.

The Company's capital resources and operations to date have been funded primarily with the proceeds from the Collaboration Agreement and private and public equity offerings. 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. The COVID-19 outbreak and mitigation measures also have had, and may continue to have, an adverse impact on global economic conditions, which could have an adverse effect on the Company's ability to raise capital when needed.

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 incorporated under the laws of England and Wales;
MeiraGTx, LLC, a Delaware limited liability company ("Meira LLC");

MeiraGTx UK II Limited, a limited company incorporated under the laws of England and Wales ("Meira UK II");
MeiraGTx Ireland DAC, a designated activity company incorporated under the laws of Ireland ("Meira Ireland");
MeiraGTx Netherlands B.V., a private company with limited liability incorporated under the laws of the Netherlands ("Meira Netherlands");
BRI-Alzan, Inc., a Delaware corporation ("BRI-Alzan");
MeiraGTx Bio Inc., a Delaware corporation ("Meira Bio");
MeiraGTx B.V., a private company with limited liability incorporated under the laws of the Netherlands ("Meira B.V.");
MeiraGTx Neurosciences, Inc., a Delaware corporation ("Meira Neuro"); and
MeiraGTx UK Limited, a limited company incorporated under the laws of England and Wales ("Meira UK").

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, share-based compensation, leases, asset retirement obligations and tax incentive receivable.

Additionally, the Company has made estimates of the impact of the COVID-19 pandemic within the consolidated financial statements and there may be changes to those estimates in future periods. Actual results may differ from these estimates.

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 employees 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, 2020 and 2019, the Company recorded reductions to research and development expenses of $5.3 million and $12.0 million, respectively.

In addition, the Company incurs Value Added Tax ("VAT") on services provided by UK, Netherlands and Ireland 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 $4.0 million and $1.8 million as of December 31, 2020 and 2019, respectively, which is included in other current assets in the accompanying consolidated balance sheet.

Foreign Currency Contracts

The Company uses foreign currency forward contracts to protect against changes in anticipated foreign currency cash flows resulting from changes in foreign currency exchange rates, primarily associated with non-functional currency denominated expenses. The Company does not designate its foreign currency forward contracts as part of a hedging transaction. Changes in the fair value are recorded each period within the Company's consolidated statement of operations and comprehensive loss as a component of net loss. There were no foreign currency forward contracts outstanding as of December 31, 2020.

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.

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The table below represents the values of the Company's financial assets and liabilities that are required to be measured at fair value on a recurring basis:

		Fair Value Measurement Using:		
Description	December 31, 2020	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Asset retirement obligations	$ 1,814,338	$ —	$ —	$ 1,814,338

		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

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 and Ireland. 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.

Intangible Assets

Intangible assets consist of purchased rights to licensed technology as it relates to the Company’s manufacturing processes and has future alternative in the Company’s operations. The licensed technology is being amortized on a straight-line basis over 7 years, which represents the estimated periods of benefit and the expected pattern of consumption (see Note 6).

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 2020 or 2019.

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.

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.

The Company uses estimates to determine the asset retirement obligations at the end of the lease term and discounts such asset retirement obligations using an estimated discount rate. Interest on the discounted asset retirement obligation is amortized over the term of the lease using the effective interest method and is recorded as interest expense in the consolidated statements of operations and comprehensive loss.

The change in asset retirement obligations is as follows:

	For the Year Ended December 31,	
	2020	2019
Balance at beginning of period	$ 1,654,755	$ 128,119
Additional asset retirement obligations during the period	—	1,270,262
Amortization of interest	136,069	20,621
Change in fair value	—	255,999
Effects of exchange rate	23,514	(20,246)
Balance at end of period	$ 1,814,338	$ 1,654,755

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 initial public offering ("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 could 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 employment, service 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.

Restricted Share Units

The Company grants restricted share units ("RSUs") to employees and non-employee consultants as compensation for services performed. Awards of RSUs 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 RSUs, 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 RSUs is determined using the closing market price of the Company's ordinary shares on the date of grant.

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 11 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, Meira Ireland, Meira Netherlands and Meira B.V. are measured using the foreign subsidiaries' local currency as the functional currency. These entities' 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, 2020 and 2019, the Company recorded unrecognized tax positions of $512,785 and $0, respectively. No interest and penalties have been accrued relative to the unrecognized tax positions.

The Company is required to estimate income taxes in each of the jurisdictions in which it operates.

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 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, 2020	December 31, 2019
Restricted share units	545,000	—
Share options	4,824,771	3,645,360
Restricted ordinary shares subject to forfeiture	—	217,726
	5,369,771	3,863,086

Other Comprehensive Loss

Other comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. The only component of other comprehensive 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 Collaboration Agreement are generated in the United Kingdom.

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

	December 31, 2020	December 31, 2019
United States	$ 17,536,207	$ 14,354,792
United Kingdom	44,487,022	39,476,700
Ireland	27,413,397	—
Netherlands	1,684,798	1,076,286
	$ 91,121,424	$ 54,907,778

Accounting Pronouncements Recently Adopted

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 adoption of the provisions of ASU 2018-13 on January 1, 2020 did not have a material impact on the current financial statements.

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 ASC 808, Collaborative Arrangements and ASC 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 adoption of ASU 2018-18 on January 1, 2020 did not have a material impact on the current financial statements.

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 adoption of ASU 2018-15 on January 1, 2020 did not have a material impact on the current 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 adoption of ASU 2019-12 did not have a material impact on the 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.

3. Acquisitions

Emrys Bio Inc.

On April 9, 2020 (the "Closing Date"), the Company acquired Emrys, a pre-clinical biopharmaceutical company developing brain-derived neurotrophic factor gene therapy for treatment of genetic obesity disorders, as well as the development of gene therapy product candidates for other central nervous system diseases. The Company acquired Emrys pursuant to an Agreement and Plan of Merger (the "Emrys Merger Agreement"), dated as of April 9, 2020, by and among the Company, Emrys, and EB Acquisition, Inc., a wholly-owned subsidiary of the Company ("Merger Sub"), the Emrys stockholders and the Emrys stockholder representative, pursuant to which Merger Sub was merged with and into Emrys, with Emrys being the surviving corporation (the "Merger"). As a result of the Merger, Emrys became a wholly-owned subsidiary of the Company and was renamed MeiraGTx Bio Inc.

As part of the entry into the Emrys Merger Agreement, the parties to the Agreement and Plan of Merger (the "Vector Merger Agreement"), dated October 5, 2018, entered into an Amendment and Waiver to the Vector Merger Agreement by and among the Company, VN Acquisition, Inc., VN Acquisition 2, Inc., the former Vector Neurosciences Inc. ("Vector") stockholders and the Vector stockholder representative, to terminate and waive all milestone payments payable under the Vector Merger Agreement that were otherwise required if specified

regulatory milestones were met, and to terminate and waive all royalty payments that were otherwise required to be paid under the Vector Merger Agreement. Several of the selling Emrys stockholders were also stockholders of Vector.

In connection with the acquisition of Emrys and the termination and waiver of the milestone and royalty payments otherwise required under the Vector Merger Agreement, the consideration to Emrys selling stockholders consisted of an aggregate of 580,000 of the Company's ordinary shares of which (i) 232,000 ordinary shares were issued on the Closing Date, (ii) 290,000 restricted ordinary shares were issued on the Closing Date, with 50% of such restricted ordinary shares scheduled to vest on each of the first and second anniversaries of the Closing Date, and (iii) 58,000 ordinary shares will be issued 18 months following the Closing Date, provided that the shares described in clauses (ii) and (iii) are subject to certain indemnification claims under the Emrys Merger Agreement. Total consideration of $7,685,001 was based on the closing price of the Company's ordinary shares of $13.25 per share on the Closing Date.

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 $7,685,001 as of April 9, 2020. 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.

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. Arthrogen was renamed MeiraGTx Netherlands B.V.

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.

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

4. Prepaid Expenses

Prepaid expenses at December 31, 2020 and 2019 consist of the following:

	December 31, 2020	December 31, 2019
Insurance	$ 2,901,728	$ 1,758,915
Clinical trial costs	1,624,873	1,349,657
Manufacturing costs	1,395,141	259,509
Dues and license fees	515,328	264,123
Rent	169,038	183,952
Research and development	164,338	239,161
Other	311,301	408,768
	$ 7,081,747	$ 4,464,085

5. Property, Plant and Equipment, net

Property, plant and equipment, net at December 31, 2020 and 2019 consist of the following:

	December 31, 2020	December 31, 2019
Leasehold improvements	$ 33,776,712	$ 17,557,316
Manufacturing equipment	7,021,162	5,647,484
Laboratory equipment	7,350,285	3,700,632
Computer and office equipment	3,712,884	1,066,984
Furniture and fixtures	567,730	441,101
	52,428,773	28,413,517
Less: Accumulated depreciation	(8,386,870)	(4,555,409)
	$ 44,041,903	$ 23,858,108

In connection with certain operating leases, the Company has determined that it has asset retirement obligations in the aggregate amount of $3,736,404 at the end of those 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 finance leases in the amount of $95,880 are included in computer and office equipment and were fully depreciated as of December 31, 2019.

Depreciation expense was $4,171,626 and $2,238,560 for the years ended December 31, 2020 and 2019 respectively.

6. Intangible Assets

In November 2020, the Company entered into a non-exclusive, royalty-free technology license agreement that required the Company to pay an upfront payment to the licensor of $2.1 million. The Company accounted for the transaction as an asset acquisition and recorded an intangible asset as it was determined to have alternative future uses in connection with the Company's manufacturing capabilities.

The following table presents the details of the Company's intangible assets as of December 31, 2020:

Type	Amortization Period	Gross Carrying Amount	Accumulated Amortization	Net
Licensed Technology	7 years	$ 2,144,541	$ 25,530	$ 2,119,011

There were no intangible assets as of December 31, 2019. For the year ended December 31, 2020, amortization expense of $25,530 was recorded as a component of research and development expenses. There was no amortization expense for the year ended December 31, 2019.

As of December 31, 2020, the expected amortization expense for the next five years and thereafter is as follows:

	Amortization Expense
2021	$ 306,360
2022	306,360
2023	306,360
2024	306,360
2025	306,360
Thereafter	587,211
Total amortization	$ 2,119,011

7. Accrued Expenses

Accrued expenses at December 31, 2020 and 2019 were comprised of the following:

	December 31, 2020	December 31, 2019
Clinical trial costs	$ 11,154,015	$ 7,788,077
Compensation and benefits	3,791,303	6,850,335
Manufacturing costs	1,885,848	125,717
Professional fees	1,219,116	486,743
Consulting	1,046,774	1,247,989
Fixed assets	948,571	1,108,362
Rent and facilities costs	662,040	283,876
Other	153,153	192,658
	$ 20,860,820	$ 18,083,757

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 and restricted share units ("RSUs") to selected officers, employees and non-employee consultants. The Company's board of directors or a committee thereof administers the Plans. Upon the adoption of the 2018 Incentive Award Plan, the Company ceased issuing awards under the 2016 Equity Incentive Plan. The number of shares available for issuance under the 2018 Incentive Award Plan are increased on January 1 of each calendar year beginning in 2019 and ending in and including 2028, by an amount equal to the lesser of (A) 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. Under the 2018 Incentive Award Plan the Company initially reserved up to 3,054,996 shares for issuance, which has been increased to 5,620,882 as of December 31, 2020. As of December 31, 2020, 1,584,468 shares remain available for future issuance. In January 2021, the number of shares available for issuance under the 2018 Incentive Award Plan increased by 1,767,566 shares. Also, in January 2021, the Company's board of directors authorized the issuance of 505,000 restricted share units to certain executives and up to 1,303,700 options to certain executives, employees and consultants, in each case, under the 2018 Incentive Award Plan.

Options

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, 2020 and 2019 is as follows:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (years)
Outstanding at December 31, 2018	3,254,365	$ 7.64	
Granted	551,000	17.94	
Exercised	(134,533)	4.14	
Expired	—	—	
Forfeited	(25,472)	9.37	
Outstanding at December 31, 2019	3,645,360	9.31	8.45 years
Granted	1,666,500	15.91	
Exercised	(109,296)	7.69	
Expired	—	—	
Forfeited	(377,793)	15.71	
Outstanding at December 31, 2020	4,824,771	$ 11.85	7.67 years
Options exercisable at December 31, 2020	2,249,113	$ 8.88	6.71 years
Aggregate intrinsic value of options outstanding as of December 31, 2020	$ 22,338,580		
Aggregate intrinsic value of options exercisable as of December 31, 2020	$ 15,365,249		

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 next annual meeting of shareholders after the date of grant.

The total fair value of options vested during the years ended December 31, 2020 and 2019 was $8,156,474 and $6,098,621, respectively.

The weighted average grant date fair value of options granted during the years ended December 31, 2020 and 2019 was $11.87 and $13.79, 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):

	2020	2019
Risk-free interest rate	0.32 - 2.56%	1.76 - 2.55%
Expected volatility	90%	90%
Expected dividend yield	0%	0%
Expected life (in years)	5.5 - 6.1	5.5 - 6.1

For the years ended December 31, 2020 and 2019, total share-based compensation expense recorded in connection with the options was $12,866,121 and $8,024,476, of which $6,975,323 and $4,338,180 was recoded as general and administrative expense and $5,890,798 and $3,686,296 was recorded as research and development expense, respectively.

As of December 31, 2020, the total compensation expense relating to unvested options granted that had not yet been recognized was $22,808,502, which is expected to be realized over a period of 3.9 years. The Company will issue shares upon exercise of options from ordinary shares reserved under the Plans.

Restricted Share Units

On January 8, 2020 and March 6, 2020, the Company granted 505,000 and 40,000 RSUs to certain members of senior management and a consultant, respectively. The RSUs were valued at $20.30 and $16.45 per share, respectively, and the related share-based compensation expense, which is recognized ratably over the requisite service period, is included in general and administrative and research and development expenses in the consolidated statements of operations and comprehensive loss. These RSUs vest 50% on the second anniversary of the date of grant and 25% on each of the third and fourth anniversaries of the date of grant.

For the year ended December 31, 2020, total share-based compensation expense recorded in connection with the RSUs was $2,643,833, of which $2,509,495 was recoded as general and administrative expense and $134,338 was recorded as research and development expense.

As of December 31, 2020, the total compensation expense relating to unvested RSUs granted that had not yet been recognized was $8,265,667, which is expected to be realized over a period of 3.2 years.

Restricted Ordinary Shares

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 $6,545,688 and $15,982,670, of which $2,906,626 and $6,531,744 was share-based and $3,639,062 and $9,450,926 was paid in cash, was recorded as general and administrative expense during the years ended December 31, 2020 and 2019, respectively (See Note 12).

A summary of the restricted ordinary shares is as follows:

	Ordinary Shares	$ Value
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
Vested during 2020	(217,726)	(3,265,890)
Non-vested at December 31, 2020	—	$ —

During the years ended December 31, 2020 and 2019 the Company recognized total share-based compensation expense in the accompanying consolidated statements of operations and comprehensive loss as follows:

	2020	2019
Research and development	$ 6,025,136	$ 5,059,046
General and administrative	12,391,444	10,869,924
Total share-based compensation	$ 18,416,580	$ 15,928,970

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, 2020 and 2019.

9. Ordinary Shares

2020

Public Offering

In November 2020, the Company issued 5,000,000 ordinary shares in a public offering for gross proceeds of $64.3 million. In December 2020, the underwriter exercised its overallotment provision and the Company issued an additional 750,000 ordinary shares for gross proceeds of $9.6 million. Offering costs in connection with both issuances were approximately $4.6 million.

At-the-Market Offering

In July 2019, the Company entered into an “at-the-market” sales agreement with Chardan Capital Markets, LLC, or Chardan, pursuant to which the Company may sell from time to time, ordinary shares having an aggregate offering price of up to $75.0 million through Chardan, acting as our agent. During the year ended December 31, 2020, the Company raised gross proceeds of $13.2 million, through the sale of 993,448 ordinary shares pursuant to an “at-the-market” equity offering program. Offering costs were approximately $0.5 million. In November 2020, the Company terminated the at-the-market equity program.

Acquisitions

In April 2020, the Company issued 522,000 ordinary shares in connection with the acquisition of Emrys Bio Inc.

In October 2020, the Company issued 22,500 ordinary shares, which represented the holdback shares from a previous acquisition.

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.

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, which was recorded as research and development expense.

On October 31, 2019, the Company issued 95,000 shares to a consultant in the amount of $1,372,750, which was recorded as research and development expense.

10. Income Taxes

For the years ended December 31, 2020 and 2019, the Company recognized a tax benefit of $0.

As of December 31, 2020, the Company had U.S. federal and state net operating losses ("NOLs") and foreign carryforward tax losses which are available to reduce future taxable income of:

	Federal	State/City
United Kingdom	$ 142,241,850	$ —
United States	$ 34,743,371	$ 34,366,051
Netherlands	$ 26,111,603	$ —
Ireland	$ 626,498	$ —

The U.S. federal and state NOLs 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. NOLs incurred after December 31, 2017 and the UK and Ireland carryforward tax losses will be indefinitely carried forward. The Netherlands carryforward tax losses expire after nine years from the date incurred prior to 2019 and six years for tax losses incurred after 2018. The net operating losses incurred in 2011 and earlier have expired as of December 31, 2020. Also, as of December 31, 2020, the Company had orphan drug and research and development credits in the U.S. in the amount of $5,127,849 which will begin to expire 2036 and research and development credits of $1,204,036 in the UK which can be carried forward indefinitely. The NOLs and carryforward tax losses are subject to review and possible adjustment by the U.S., UK, Netherlands, Ireland and state tax authorities. The U.S. NOLs and UK carryforward tax

losses may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders, as defined under Section 382 Internal Revenue Code, as well as CTA 2010 Part 14 under the UK tax rules. This could limit the amount of NOLs and carryforward tax losses that the Company can utilize annually to offset future taxable income or tax liabilities. As of December 31, 2019, 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 April 2016 and again in June 2018. The Company is still in the process of determining the annual limitation on losses that occurred prior to June 2018. Netherlands has anti-abuse rules that potentially restrict the use of NOLs in certain change of control situations. Subsequent ownership changes and proposed future changes to the UK, the U.S. or the Netherlands tax rules in respect of the utilization of losses carried forward may further affect the limitation in future years, if any. The Company has completed a study on the completeness of the U.S. orphan drug and research and development credit and the results are included in the income tax footnote in 2020.

The Company's pre-tax earnings are as follows:

	December 31, 2020	December 31, 2019
United Kingdom	$ (41,372,993)	$ (37,993,537)
United States	(13,472,052)	(16,303,213)
Netherlands	(2,471,442)	(449,485)
Ireland	(675,517)	—
	$ (57,992,004)	$ (54,746,235)

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, 2020		December 31, 2019	
Statutory rate	(11,018,481)	19.00 %	(10,401,785)	19.00 %
Permanent differences - other	1,976,028	(3.41)%	(411,651)	0.75 %
RTP and other adjustment	(2,135,978)	3.68 %	3,068,999	(5.61)%
State and local rate, net of federal tax	(1,478,111)	2.55 %	(2,041,097)	3.73 %
U.K. tax credit	574,161	(0.99)%	1,278,072	(2.33)%
U.S. tax credit	(1,242,356)	2.14 %	(1,257,481)	2.30 %
Foreign tax rate differential	(254,199)	0.44 %	(347,301)	0.63 %
UK rate change (19% & 17% at expected DTA turn)	(2,233,752)	3.85 %	362,092	(0.66)%
US state rate change	25,041	(0.04)%	—	- %
Change in valuation allowance	15,787,647	(27.22)%	9,750,152	(17.81)%
Actual income tax benefit effective tax rate	—	0.00 %	—	0.00 %

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

	December 31, 2020	December 31, 2019
Current Tax Expense/(Benefit)		
United Kingdom	—	—
United States	—	—
Netherlands	—	—
Ireland	—	—
Total Current	—	—
Deferred Tax Expense/(Benefit)		
United Kingdom	(9,197,319)	(3,036,498)
United States	(5,851,708)	(6,631,936)
Netherlands	(674,817)	(81,718)
Ireland	(63,803)	—
Total Deferred	(15,787,647)	(9,750,152)
Change in Valuation Allowance	15,787,647	9,750,152
Total Income Tax Expense/(Benefit)	—	—

Deferred Tax Assets/(Liabilities)

	December 31, 2020	December 31, 2019
Deferred Tax Assets:		
Net operating loss carryforwards	$ 43,831,308	$ 31,929,792
Lease liability	6,150,436	6,012,466
R&D credit	5,819,100	2,635,188
Share-based compensation	5,392,358	2,831,696
Other	298,462	374,507
Deferred tax assets	61,491,664	43,783,649
Deferred Tax Liabilities:		
Indefinite-lived intangibles	(173,431)	(173,431)
Depreciation	(2,252,190)	(624,361)
Right of use assets	(5,928,527)	(5,635,987)
Less: valuation allowance	(53,310,947)	(37,523,301)
Net deferred tax liability	$ (173,431)	$ (173,431)

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, 2020 and 2019 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. The UK had previously enacted its statutory rate to be reduced to 17% as of

April 1, 2020, but amending legislation was enacted in 2020 such that this reduction did not take effect. As the Company does not expect to be able to utilize its carryforward tax losses 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 19%.

As of December 31, 2020 and 2019, the Company recorded unrecognized tax positions of $512,785 and zero respectively. The unrecognized tax positions are netted with deferred tax assets above with full valuation allowance. The changes to unrecognized tax positions for 2020 and 2019 were as follows:

	December 31, 2020	December 31, 2019
Unrecognized tax benefits as of January 1	$ —	$ —
Gross increases/(decreases) related to current year	138,040	—
Gross increases/(decreases) related to prior years	374,745	—
Foreign currency translation	—	—
Unrecognized tax positions as of December 31	$ 512,785	$ —

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2020 and 2019, 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, Netherlands and Ireland and various state jurisdictions. In the U.S., all years remain subject to examination. The earliest year subject to the statute of limitations in the UK is 2018. The statute of limitations in the Netherlands is generally 5 years after the end of the taxable year. In Ireland, the Irish Revenue may undertake an audit of a company’s tax return within a period of four years from the end of the accounting period in which the return is submitted.

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.

New Tax Legislation

Many governments have enacted or are currently contemplating economic stimulus and financial aid measures. Many of these measures include deferring the due dates for tax payments, including both income tax and other taxes. The Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") was enacted on March 27, 2020 in the United States to address the economic impacts of the COVID-19 pandemic. The CARES Act includes corporate income tax, payroll tax, and other provisions. While the Company may receive financial, tax, or other benefits under the bill, this legislation did not impact the Company during the year ended December 31, 2020.

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 facilities 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 years ended December 31, 2020 and 2019, the Company recognized $15,562,985 and $13,291,956, respectively, of the deferred revenue – related party as license revenue.

The Company also recognized $63,003,824 and $27,296,062 during the years ended December 31, 2020 and 2019, respectively, related to the reimbursement of research and development expenses, of which $57,407,089 and $27,296,062, respectively, was recorded as an offset to research and development expenses and $5,596,735 and $0, respectively, was recorded as an offset to prepaid expenses.

As of December 31, 2020, the Company expects to recognize the remaining $72,841,777 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 4.5 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	(493,953)
Deferred revenue at December 31, 2019	86,214,091
Deferred revenue recognized as license revenue during the year ended December 31, 2020	(15,562,985)
Effects of exchange rate	2,190,671
Deferred revenue at December 31, 2020	$ 72,841,777

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. In October 2020, the master services agreement was extended for an additional four years. Pursuant to a task order to the master services agreement, UCL Consultants Limited had provided pre-clinical research and development under the direction of the Company. The services rendered under the task order were completed in 2020.

Total research and development expenses under this agreement for the years ended December 31, 2020 and 2019 was approximately $203,000 and $306,000, respectively.

There are currently no future obligations under the agreement as of December 31, 2020. The amount due to UCL under the master services agreement at December 31, 2020 and 2019 is $0 and $166,404, 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 $54.4 million using the exchange rate at December 31, 2020, 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.

Effective March 23, 2020, the Company entered into another worldwide license agreement with UCL Business, to develop an additional ocular gene therapy technology. Under the terms of the agreement, the Company agreed to pay UCL Business certain development and sales milestone payments, if achieved, in the aggregate amount of $39.25 million and royalties on net sales, as defined upon commercialization. Additionally, the Company is responsible for all patent prosecution and maintenance costs incurred and also agreed to pay UCL Business an upfront payment of $50,000 and an annual maintenance fee of $25,000 until the first commercial sale of a product. The agreement terminates upon the later of (i) the last valid claim in a relevant product, or (ii) the 10th anniversary of the first commercial sale of a product.

The Company incurred research and development expenses under the agreements in the amount of $273,180 and $4,271,275, inclusive of the amendment payments of approximately $0, and $3,942,000 during the years ended December 31, 2020 and 2019, 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 provided for monthly base rent and property management fees, including rent escalations and rent holidays, plus operating expenses during the lease term, which was scheduled to expire on December 31, 2021. The Company recorded monthly rent expense on a straight-line basis from July 1, 2016 through February 29, 2020, the date the ARE Lease was terminated as described below.

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. Accordingly, the remaining right of use asset and operating lease liability in the amount of $825,888 and $969,478, respectively, was written off which resulted in a gain of $143,590.

Total rent expense under this operating lease was $81,260 and $487,555 for the years ended December 31, 2020 and 2019, respectively.

In connection with the signing of this lease, the Company entered into a standby letter of credit agreement for $122,866, which served as a security deposit for the premises. The standby letter of credit was released in May 2020.

Kadmon Lease

The Company leases office space on a month-to-month basis from Kadmon Corporation, LLC ("Kadmon").

During the years ended December 31, 2020 and 2019, the Company incurred rent charges from Kadmon in the amount of $597,740 and $576,404, respectively, which are included in loss from operations.

During the years ended December 31, 2020 and 2019, the Company made cash payments totaling $597,740 and $576,404, respectively, to Kadmon. There were no amounts due to Kadmon at December 31, 2020 and 2019.

12. Leases

The Company has commitments under operating leases for laboratory, warehouse, clinical trial sites 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 191 years. Certain lease agreements contain provisions for future rent increases. Payments due under the lease contracts include fixed payments.

Total rent expense recorded under these leases was $3,341,535 and $1,776,631 for the years ended December 31, 2020 and 2019, respectively.

As of December 31, 2020, the Company has short term lease commitments amounting to approximately $56,000 on a monthly basis for two leases for office space that are month-to-month leases.

On August 4, 2020, Meira Ireland entered into two agreements (the "Agreements") with Shannon Commercial Enterprises DAC trading as Shannon Commercial Properties, to acquire two properties in the Shannon Free Zone in Shannon, Ireland for an aggregate price of €18 million, or approximately $21.2 million. These properties will serve as the Company's second cGMP viral vector manufacturing facility and its first cGMP plasmid and DNA production facility.

The closing for the first building occurred on August 27, 2020. The total cost of the first building, including taxes and legal fees, was €11,890,000, or approximately $13,801,007, and has been recorded as a right of use asset in the consolidated balance sheets as of December 31, 2020. There is no corresponding lease liability as the Company paid the full cost on the date of the closing.

The closing for the second building occurred in January 2021. At the closings, Meira Ireland entered into a lease for each property providing for a long leasehold interest of approximately 191 years.

The leases also include customary terms and conditions, with a nominal annual lease cost and annual maintenance fees of approximately €31,000, or approximately $37,000, in the aggregate, which amount is subject to change depending on the annual maintenance costs within the Shannon Free Zone development.

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

The components of lease cost for the years ended December 31, 2020 and 2019 are as follows:

	2020	2019
Finance lease cost		
Amortization of right-of-use assets	$ 519,379	$ 300,229
Interest on lease liabilities	3,081	2,409
Total finance lease cost	522,460	302,638
Operating lease cost	3,422,795	2,384,048
Short-term lease cost	714,172	1,282,709
Total lease cost	$ 4,659,427	$ 3,969,395

Amounts reported in the consolidated balance sheets for leases where the Company is the lessee as of December 31, 2020 and 2019 were as follows:

	December 31, 2020	December 31, 2019
Operating leases		
Right-of-use asset	$ 21,485,924	$ 21,857,600
Capitalized lease obligations	$ 22,220,515	$ 23,127,813
Finance leases		
Right-of-use asset	$ 21,596,435	$ 7,144,848
Capitalized lease obligations	$ 28,325	$ 50,737
Weighted-average remaining lease term		
Operating leases	7.0 years	7.9 years
Finance leases	175.1 years	107.0 years
Weighted-average discount rate		
Operating leases	8.6 %	8.5 %
Finance leases	8.0 %	7.3 %

Other information related to leases as of the years ended December 31, 2020 and 2019 are as follows:

	2020	2019
Cash paid for amounts included in the measurement of lease liabilities		
Operating cash flows from finance leases	$ 21,604	$ 28,187
Operating cash flows from operating leases	$ 3,790,734	$ 1,246,169
Financing cash flows from finance leases	$ 3,081	$ 2,355
Right-of-use assets obtained in exchange for lease liabilities		
Operating leases	$ 1,889,065	$ 23,279,980
Finance leases	$ —	$ 44,629

Future minimum lease payments under non-cancellable leases as of December 31, 2020 are as follows:

	Operating Leases	Finance Leases
2021	$ 4,383,995	$ 17,505
2022	4,475,018	13,129
2023	4,566,431	—
2024	4,405,144	—
2025	4,381,270	—
Thereafter	7,151,280	—
Total undiscounted lease payments	$ 29,363,138	$ 30,634
Less: Imputed interest	(7,142,623)	(2,309)
Total lease liabilities	$ 22,220,515	$ 28,325

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 per year, which was increased to a maximum aggregate amount of £430,000 per year, or approximately $587,000, for the year ended December 31, 2020. 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. In May 2019 one of the senior officers resigned from the Company and in May 2020, the resignation became effective. For the years ended December 31, 2020 and 2019, the Company recorded £935,958 and £944,500 or approximately $1,278,425 and $1,234,000, respectively, in research and development costs under these agreements. Future obligations to be paid under the remaining agreement equals £120,000, or approximately $164,000 at December 31, 2020.

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 per year. 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.

Bonuses granted to the senior officers, which included their guaranteed and discretionary bonuses, for the years ended December 31, 2020 and 2019, in the aggregate amount of $3,300,000 and $5,403,000, respectively.

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 employment agreements equal $2,418,750, as of December 31, 2020.

Research Agreements

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, 2020 and 2019 were $379,478 and $1,756,487, respectively. There are no future obligations to be paid under the agreements.

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, 2020 and 2019 were $0 and $60,000, 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 were $15,000 for each of the years ended December 31, 2020 and 2019.

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.

Netherlands

Meira Netherlands 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.

Ireland

On November 20, 2020, MeiraGTx Ireland adopted a defined contribution pension plan. All MeiraGTx Ireland employees are eligible to participate in the plan upon joining the Company. All eligible employees, if they elect to join the pension scheme, receive an employer pension contribution. The Company's current contribution, exclusive of an employee match, is 4.5%, which exceeds Revenue Ireland requirements.

During the years ended December 31, 2020 and 2019, employer contributions to all plans were $1,089,657 and $604,294, respectively.

15. Subsequent Events

Visiogene LLC

On January 4, 2021, the Company and Visiogene LLC ("Visiogene") entered into a License and Investment Agreement for an exclusive, worldwide license to certain of Visiogene's intellectual property relating to ocular gene therapy and acquired Visiogene preferred units for total consideration of $5.0 million in cash, with the majority of such payment being allocated toward the research and development of novel products, and the issuance to Visiogene of 75,000 ordinary shares of the Company.

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, 2020. 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, 2020.

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, 2020 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 2021 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item is incorporated by reference to our definitive proxy statement for our 2021 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

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, 2020)

The following table provides information as of December 31, 2020, 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)	1,385,192	$ 5.45	—
2018 Plan (2)(3)	3,984,579	$ 14.43	1,584,468
2018 ESPP (4)	—	—	1,150,637
Equity compensation plans not approved by shareholders	—	—	—
Total	5,369,771	$ 11.85	2,735,105

(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) The weighted average exercise price of outstanding awards does not take into account the shares issuable upon vesting of outstanding restricted share units which have no exercise price. At December 31, 2020 there were a total of 545,000 shares subject to restricted share units.

(4) 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 2021 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

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 2021 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this Item is incorporated by reference to our definitive proxy statement for our 2021 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2020.

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	10-K	001-38520	4.2	3/11/20	
4.3	Description of Securities	10-K	001-38520	4.3	3/11/20	
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#	Form of Change in Control Agreement.					*
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				Filed/ Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
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 January 7, 2020, between MeiraGTx Holdings plc and Bruce Gottlieb.	10-Q	001-38520	10.1	5/7/20	
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-K	001-38520	10.30	3/11/20	
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.	10-K	001-38520	10.31	3/11/20	
10.32	Particulars and Conditions of Sale of Building 2, Block K, Shannon Free Zone, Shannon, County Clare, Ireland, dated as of August 4, 2020, by and between Shannon Commercial Enterprises DAC trading as Shannon Commercial Properties and MeiraGTx Ireland DAC, including agreed form of Lease between Shannon Commercial Enterprises DAC and MeiraGTx Ireland DAC.	10-Q	001-38520	10.1	11/5/20	
10.33	Particulars and Conditions of Sale of Building 3, Block K, Shannon Free Zone, Shannon, County Clare, Ireland, dated as of August 4, 2020, by and between Shannon Commercial Enterprises DAC trading as Shannon Commercial Properties and MeiraGTx Ireland DAC, including agreed form of Lease between Shannon Commercial Enterprises DAC and MeiraGTx Ireland DAC.	10-Q	001-38520	10.2	11/5/20	
21	List of Subsidiaries					*

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
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	Inline XBRL Instance Document.					*
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					*
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					*
101.DEF	Inline XBRL Taxonomy Definition Linkbase Document.					*
101.LAB	Inline XBRL Taxonomy Label Linkbase Document.					*
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					*
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					*

* 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, 2021

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 Alexandria Forbes, Ph.D	President and Chief Executive Officer and Director (Principal Executive Officer)	March 11, 2021
/s/ Richard Giroux Richard Giroux	Chief Financial Officer (Principal Financial and Accounting Officer)	March 11, 2021
/s/ Keith R. Harris, Ph.D. Keith R. Harris, Ph.D.	Chairman of the Board and Director	March 11, 2021
/s/ Martin Indyk Martin Indyk	Director	March 11, 2021
/s/ Ellen Hukkelhoven Ellen Hukkelhoven	Director	March 11, 2021
/s/ Nicole Seligman Nicole Seligman	Director	March 11, 2021
/s/ Arnold J. Levine, Ph.D. Arnold J. Levine, Ph.D.	Director	March 11, 2021
/s/ Joel S. Marcus Joel S. Marcus	Director	March 11, 2021
/s/ Lord Mendoza Lord Mendoza	Director	March 11, 2021
/s/ Thomas E. Shenk, Ph.D. Thomas E. Shenk, Ph.D.	Director	March 11, 2021

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 $66,000 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 $30,000 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.

* * * * *

Exhibit 10.14

CHANGE IN CONTROL AGREEMENT

This Change in Control Agreement ("***Agreement***") is made effective as of [_____], by and between [EMPLOYING SUBSIDIARY] (the "***Company***") and [_____] ("***Executive***").

WHEREAS, Executive is a key employee of the Company;

WHEREAS, the Company recognizes that the possibility of a change in control and a related involuntary termination raises uncertainty and questions among key employees and can be a distraction to the Executive to the detriment of the Company, Parent (as defined below) and its shareholders; and

WHEREAS, the Company believes that it is in the best interests of the Company, Parent and its shareholders to provide the Executive with an incentive to motivate the Executive to maximize the value of the Company upon a Change in Control (as defined below) for the benefit of shareholders, and to induce the Executive to remain in the employ of the Company.

NOW, THEREFORE, in consideration of the foregoing recitals and the mutual promises, terms, provisions and conditions set forth in this Agreement, the Company and the Executive hereby agree as follows:

1. Definitions. For purposes of this Agreement, the following terms shall have the following meanings:

(a) "***Affiliate***" means with respect to any person or entity, any other person or entity that, directly or indirectly, through one or more intermediaries, controls, or is controlled by, or is under common control with, such person or entity. For purposes of this definition, "control", when used with respect to any person or entity, means the power to direct the management and policies of such person or entity, directly or indirectly, whether through ownership of voting securities, by contract or otherwise, and the terms "controlling" and "controlled" have meanings correlative to the foregoing.

(b) "***Base Salary***" means Executive's annual base salary at the rate in effect from time to time.

(c) "***Board***" means the Board of Directors of Parent.

(d) "***Cause***" means any of the following: (i) Executive's commission of an act of fraud, embezzlement or theft against the Company or its Affiliates; (ii) Executive's conviction of, or plea of no contest to, a felony or crime involving moral turpitude; (iii) Executive's refusal to perform material duties as an employee of the Company, which to the extent curable, remains uncured for 30 days following Executive's receipt of written notice thereof; (iv) Executive's material breach of any material policy of the Company or any of its Affiliates that is applicable to Executive or of any material agreement with the Company or any of its Affiliates, including the Confidentiality and Restrictive Covenant Agreements, which to the extent curable, remains uncured for 30 days following Executive's receipt of written notice thereof; (v) Executive's gross negligence, willful misconduct or any other act of willful disregard for the Company's or any of its Affiliates' best interests; or (vi) Executive's refusal to cooperate with a governmental or internal investigation of the Company or any of its Affiliates, or its or their directors, officers or employees. Notwithstanding anything in this Agreement or the MeiraGTx Holdings plc 2018 Incentive Award Plan (the "***2018 Plan***") to the contrary, this Agreement shall be deemed a "Relevant Agreement" for purposes of the 2018 Plan

such that the definition of "Cause" set forth in this Agreement shall apply over any alternate definition of "Cause" set forth in the 2018 Plan.

(e) "***Change in Control***" means and includes each of the following:

(i) A transaction or series of transactions (other than an offering of Ordinary Shares to the general public through a registration statement filed with the Securities and Exchange Commission or a transaction or series of transactions that meets the requirements of clauses (A) and (B) of subsection (iii) below) whereby any "person" or related "group" of "persons" (as such terms are used in Sections 13(d) and 14(d)(2) of the Exchange Act) (other than Parent, any of its subsidiaries, an employee benefit plan maintained by Parent or any of its subsidiaries or a "person" that, prior to such transaction, directly or indirectly controls, is controlled by, or is under common control with, Parent) directly or indirectly acquires beneficial ownership (within the meaning of Rule 13d-3 under the Exchange Act) of securities of Parent possessing more than 50% of the total combined voting power of Parent's securities outstanding immediately after such acquisition; or

(ii) During any period of two consecutive years, individuals who, at the beginning of such period, constitute the Board together with any new Director(s) (other than a Director designated by a person who shall have entered into an agreement with Parent to effect a transaction described in subsections (i) or (iii)) whose election by the Board or nomination for election by Parent's shareholders was approved by a vote of at least two-thirds of the Directors then still in office who either were Directors at the beginning of the two-year period or whose election or nomination for election was previously so approved, cease for any reason to constitute a majority thereof; or

(iii) The consummation by Parent (whether directly involving Parent or indirectly involving Parent through one or more intermediaries) of (x) a merger, consolidation, reorganization, or business combination or (y) a sale or other disposition of all or substantially all of Parent's assets in any single transaction or series of related transactions or (z) the acquisition of assets or stock of another entity, in each case other than a transaction:

(A) which results in Parent's voting securities outstanding immediately before the transaction continuing to represent (either by remaining outstanding or by being converted into voting securities of Parent or the person that, as a result of the transaction, controls, directly or indirectly, Parent or owns, directly or indirectly, all or substantially all of Parent's assets or otherwise succeeds to the business of Parent (Parent or such person, the "***Successor Entity***")) directly or indirectly, at least a majority of the combined voting power of the Successor Entity's outstanding voting securities immediately after the transaction, and

(B) after which no person or group beneficially owns voting securities representing 50% or more of the combined voting power of the Successor Entity; provided, however, that no person or group shall be treated for purposes of this clause (B) as beneficially owning 50% or more of the combined voting power of the Successor Entity solely as a result of the voting power held in Parent prior to the consummation of the transaction.

Notwithstanding the foregoing, if a Change in Control constitutes a payment event with respect to any payment or benefits (or portion thereof) that provides for the deferral of compensation that is subject to Section 409A, to the extent required to avoid the imposition of additional taxes under Section 409A, the transaction or event described in subsection (i), (ii) or (iii) with respect to such

payment or benefits (or portion thereof) shall only constitute a Change in Control for purposes of the payment timing of such payment or benefits if such transaction also constitutes a "change in control event," as defined in Treasury Regulation Section 1.409A-3(i)(5).

(f) "***CIC Qualifying Termination***" means Executive's Qualifying Termination which occurs during the period beginning on the date that is [two (2) weeks] prior to a Change in Control and ending on the date that is [twelve (12) months] following a Change in Control (the "***Protected Period***"); provided that, with respect to a Qualifying Termination that occurs prior to a Change in Control, it is reasonably demonstrated that such termination (i) was at the request of a third party who had taken steps reasonably calculated or intended to effect such Change in Control, or in the case of termination by Executive for Good Reason, the circumstance or event which constitutes Good Reason occurs at the direction of such third party or (ii) otherwise arose in connection with or anticipation of such Change in Control.

(g) "***Code***" means the Internal Revenue Code of 1986, as amended, and the Treasury Regulations and other interpretive guidance thereunder.

(h) "***Confidentiality and Restrictive Covenant Agreements***" means any non-disclosure, confidentiality, invention assignment, non-competition, non-solicitation or other similar covenant or obligation of Executive under any written agreement with the Company or any of its Affiliates, as in effect from time to time, including under any employment agreement.

(i) "***Director***" means a Board member.

(j) "***Disability***" means, at any time the Company or any of its Affiliates sponsors a long-term disability plan for the benefit of the Company's employees, "disability" as defined in such long-term disability plan for the purpose of determining a participant's eligibility for benefits, provided, however, if the long-term disability plan contains multiple definitions of disability, "Disability" shall refer to that definition of disability which, if Executive qualified for such disability benefits, would provide coverage for the longest period of time. The determination of whether Executive has a Disability will be made by the person or persons required to make disability determinations under the long-term disability plan. If, at any time the Company and its Affiliates do not sponsor a long-term disability plan for the Company's employees, Disability shall mean Executive's absence from the full-time performance of Executive's duties with the Company for 180 consecutive calendar days as a result of incapacity due to mental or physical illness which is determined to be total and permanent by a physician selected by the Company or its insurers and approved by Executive or Executive's legal representative (such approval not to be unreasonably withheld, conditioned or delayed).

(k) "***Exchange Act***" means the Securities Exchange Act of 1934, as amended.

(l) "***Good Reason***" means the occurrence of any of the following events or conditions without Executive's written consent: (i) a decrease of more than 25% in Executive's Base Salary; (ii) a decrease of more than 25% in Executive's Target Bonus Amount; (iii) a material diminution in Executive's authority, duties or responsibilities as an executive and/or officer of the Company or the assignment of duties to the Executive inconsistent with those of an executive and/or officer of the Company, other than as a result of a Change in Control immediately after which Executive holds a position with the Company or its successor (or any other entity that owns substantially all of the Company's business after such sale) that is substantially equivalent with respect to the Company's business as Executive held immediately prior to such Change in Control; (iv) a change in the geographic location of Executive's principal place of employment to any location that is

more than 30 miles from the principal place of Executive's employment immediately prior to such change; or (v) the Company's material breach of a material agreement with Executive, including the Company's failure to obtain an agreement from any successor to all or substantially all of the business or assets of the Company or Parent to assume this Agreement as contemplated in Section 6(a); provided that (I) Executive must notify the Company of the occurrence of any of the foregoing events or conditions in writing within 90 days of the occurrence of such event, (II) such event or condition must, if curable, remain uncured for 30 days following the Company's receipt of such written notice (the "***Cure Period***") and (III) Executive's termination for Good Reason must occur within 90 days following the expiration of the Cure Period.

(m) "***Ordinary Shares***" means the ordinary shares of Parent.

(n) "***Parent***" means MeiraGTx Holdings plc.

(o) "***Qualifying Termination***" means a termination of Executive's employment with the Company by the Executive for Good Reason or by the Company other than for Cause, death or Disability.

(p) "***Section 409A***" means Section 409A of the Code and the regulations and guidance promulgated thereunder.

(q) ***"Target Bonus Amount***" means Executive's target annual bonus amount in effect from time to time.

2. Severance.

(a) Severance Upon Qualifying Termination. If Executive has a CIC Qualifying Termination, then subject to (x) the requirements of this Section 2, (y) the Executive's continued compliance with the Confidentiality and Restrictive Covenant Agreements and (z) the terms of Section 6, Executive shall be entitled to receive the following payments and benefits:

(i) The Company shall pay to Executive (A) Executive's earned but unpaid Base Salary through the date of Executive's termination of employment and (B) any other amounts or benefits, if any, under the Company's employee benefit plans, programs or arrangements to which Executive may be entitled pursuant to the terms of such plans, programs or arrangements or applicable law, payable in accordance with the terms of such plans, programs or arrangements or as otherwise required by applicable law (collectively, the "***Accrued Rights***");

(ii) Any unpaid annual bonus earned by Executive for the year prior to the year in which the Qualifying Termination occurs, as determined by the Board based upon actual performance achieved, which annual bonus, if any, shall be paid to Executive at substantially the same time annual bonuses for such year are paid to similarly situated active employees of the Company, but in no event later than December 31 of the year in which the Qualifying Termination occurs;

(iii) A cash severance payment equal to [one (1)] times the sum of (A) Executive's Base Salary and (B) Executive's Target Bonus Amount, payable in a lump sum on the Company's first ordinary payroll date occurring after the effective date of the Release (as defined below), but in no event later than March 15 of the year following the year in which Executive's Qualifying Termination occurs (for purposes of calculating the Executive's severance payment under this clause (iii), the Executive's Base Salary and Target Bonus Amount shall be calculated based on the rate in effect prior to any decrease that would give the Executive the right to resign for Good Reason);

(iv) If applicable to Executive and Executive timely elects continued medical, dental and/or vision coverage for Executive and Executive's covered spouse or dependents under the Company's group health plans following such Qualifying Termination in accordance with COBRA, then the Company shall pay the COBRA premiums necessary to continue Executive's and Executive's covered spouse and dependents' medical, dental and/or vision insurance coverage that is no less favorable than the more favorable of the insurance coverage in effect immediately prior to the Change in Control and the insurance coverage in effect on the date of Executive's Qualifying Termination (as applicable, the "***COBRA Premium***") until the earliest of (A) [one (1) year] following such Qualifying Termination, (B) the date when Executive becomes eligible for health insurance coverage from a new employer (and Executive agrees to promptly notify the Company of such eligibility) and (C) the date Executive ceases to be eligible for COBRA continuation coverage for any reason (the "***Benefit Continuation Period***"); provided that, if at any time the Company determines that it cannot provide the foregoing benefit without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act) or incurring an excise tax, the Company will instead pay to Executive during the remainder of the Benefit Continuation Period a taxable monthly payment equal to 140% of the COBRA Premium (based on the COBRA Premium for the first month of the Benefit Continuation Period); and

(v) All of Executive's unvested equity or equity-based awards under any equity compensation plans of Parent that vest solely based upon Executive's continued employment or service shall immediately become 100% vested on the later of the date of Executive's Qualifying Termination and the Change in Control (for the avoidance of doubt, with any such awards that vest in whole or in part based upon the attainment of performance vesting conditions being governed by the terms of the applicable award agreement) and, to the extent necessary, any unvested Parent equity awards will remain outstanding and eligible to vest following Executive's Qualifying Termination if a Change in Control occurs within [two (2) weeks] following Executive's Qualifying Termination.

(b) Other Terminations. This Agreement provides no compensation or benefits in connection with terminations which occur at times other than during the Protected Period, except that the Company shall pay to Executive the Accrued Rights upon any termination of employment.

(c) Release. As a condition to Executive's receipt of any payment or benefits under Section 2(a) other than the Accrued Rights, Executive shall execute and not revoke a general release of all claims in favor of the Company (the "***Release***") in a form substantially similar to the form attached hereto as Exhibit A, or such equivalent form as is required to comply with local employment laws applicable to Executive (and any statutorily prescribed revocation period applicable to such Release shall have expired) within the 60 day period following Executive's Qualifying Termination.

(d) Certain Reductions. Notwithstanding anything herein to the contrary, Executive's severance benefits under this Agreement shall be reduced, but not below zero, on a dollar-for-dollar (or other applicable currency) basis by the amount of any other severance payment or benefits, pay in lieu of notice, or other similar benefits payable to the Executive by the Company in connection with the Executive's Qualifying Termination, including but not limited to payments or benefits pursuant to (i) any applicable legal requirement, including any entitlement to statutory severance pay or (ii) any Company agreement, arrangement, policy or practice other than this Agreement relating to the Employee's termination of employment with the Company.

(e) Parachute Payments.

(i) Notwithstanding any other provisions of this Agreement, in the event that any payment or benefit by the Company or otherwise to or for the benefit of Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise (all such

payments and benefits, including the payments and benefits under Section 2(a), being hereinafter referred to as the "***Total Payments***"), would be subject (in whole or in part) to the excise tax imposed by Section 4999 of the Code (the "***Excise Tax***"), then the Total Payments shall be reduced (in the order provided in Section 2(e)(ii)) to the minimum extent necessary to avoid the imposition of the Excise Tax on the Total Payments, but only if the net amount of such Total Payments, as so reduced (and after subtracting the net amount of federal, state and local income and employment taxes on such reduced Total Payments and after taking into account the phase out of itemized deductions and personal exemptions attributable to such reduced Total Payments), is greater than or equal to the net amount of such Total Payments without such reduction (but after subtracting the net amount of federal, state and local income and employment taxes on such Total Payments and the amount of the Excise Tax to which Executive would be subject in respect of such unreduced Total Payments and after taking into account the phase out of itemized deductions and personal exemptions attributable to such unreduced Total Payments).

(ii) The Total Payments shall be reduced in the following order: (i) first, a reduction of any portion of the Total Payments that are exempt from Section 409A in a manner the Company reasonably determines will provide Executive with the greatest post-reduction economic benefit and (ii) second, a reduction of any portion of the Total Payments that are subject to Section 409A on a pro-rata basis or such other manner that complies with Section 409A, as reasonably determined by the Company.

(iii) All determinations regarding the application of this Section 2(e) shall be made by an accounting firm or consulting group with experience in performing calculations regarding the applicability of Section 280G of the Code and the Excise Tax selected by the Company (the "***Independent Advisors***"). For purposes of the determinations, no portion of the Total Payments shall be taken into account which, in the opinion of the Independent Advisors, (i) does not constitute a "parachute payment" within the meaning of Section 280G(b)(2) of the Code (including by reason of Section 280G(b)(4)(A) of the Code) or (ii) constitutes reasonable compensation for services actually rendered, within the meaning of Section 280G(b)(4)(B) of the Code, in excess of the "base amount" (as defined in Section 280G(b)(3) of the Code) allocable to such reasonable compensation. The costs of obtaining such determination and all related fees and expenses (including related fees and expenses incurred in any later audit) shall be borne by the Company.

(iv) In the event it is later determined that a greater reduction in the Total Payments should have been made to implement the objective and intent of this Section 2(e), the excess amount shall be returned promptly by Executive to the Company.

(f) Withholding. All compensation and benefits to Executive hereunder shall be reduced by all federal, state, local and other withholdings and similar taxes and payments required by applicable law.

(g) Notice of Termination. Any termination of the Executive's employment by the Company or by Executive under this Agreement shall be communicated by a written notice to the other party hereto (i) indicating the specific termination provision in this Agreement relied upon, (ii) setting forth in reasonable detail the facts and circumstances claimed to provide a basis for termination of the Executive's employment under the provision so indicated and (iii) specifying a date of termination (a "***Notice of Termination***"). A Notice of Termination submitted by one party may provide for a date of termination on the date the other party receives the Notice of Termination or any date thereafter elected by the first party in its discretion; *provided, however*, that in the event that Executive delivers a Notice of Termination to the Company, the Company may, in its sole discretion, change the date of termination to any date that occurs on or following the date of the Company's receipt of such Notice of Termination and is prior to the date specified in such Notice of Termination. The failure by the Company or Executive to set forth in the Notice

of Termination any fact or circumstance which contributes to a showing of Cause or Good Reason shall not waive any right of such party hereunder or preclude such party from asserting such fact or circumstance in enforcing such party's rights hereunder.

3. Condition to Severance Obligations. The Company shall be entitled to cease all severance payments and benefits to Executive in the event of Executive's breach of any of the provisions of the Confidentiality and Restrictive Covenant Agreements, which are hereby incorporated by reference into this Agreement.

4. Agreement to Arbitrate. Any controversy, claim or dispute arising out of or relating to this Agreement, shall be settled solely and exclusively by binding arbitration in New York, NY. Such arbitration shall be conducted in accordance with the then prevailing JAMS Streamlined Arbitration Rules & Procedures, with the following exceptions if in conflict: (a) one arbitrator shall be chosen by JAMS; (b) each party to the arbitration will pay its pro rata share of the expenses and fees of the arbitrator, unless otherwise required to enforce this Section 4; and (c) arbitration may proceed in the absence of any party if written notice (pursuant to the JAMS' rules and regulations) of the proceedings has been given to such party. Each party shall bear its own attorneys' fees and expenses. The parties agree to abide by all decisions and awards rendered in such proceedings. Such decisions and awards rendered by the arbitrator shall be final and conclusive. All such controversies, claims or disputes shall be settled in this manner in lieu of any action at law or equity; provided, however, that nothing in this section shall be construed as precluding the bringing an action in a court of competent jurisdiction to enforce the Confidentiality Agreements or any other non-competition, non-solicitation, non-disparagement, confidentiality, assignment of invention or other intellectual property related covenants contained in any other agreement between Executive and the Company.

5. Employment Relationship.

(a) Except as otherwise provided in Section 5(b), if applicable, Executive's employment with the Company is at-will and not for any specified period and may be terminated at any time, with or without Cause or advance notice, by either Executive or the Company, subject to the notice requirements of this Agreement or as otherwise provided in any employment agreement or other written agreement between Executive and the Company. Any change to the at-will employment relationship must be by specific, written agreement signed by Executive and an authorized representative of the Company. Nothing in this Agreement is intended to or should be construed to contradict, modify or alter this at-will relationship.

(b) Notwithstanding Section 5(a), if Executive is employed in the U.K., Executive's employment with the Company remains governed by the terms of Executive's employment agreement or other written agreement between Executive and the Company. Nothing in this Agreement is intended to or should be construed to contradict, modify or alter that employment agreement or other written agreement.

6. General Provisions.

(a) Successors and Assigns. The rights of the Company under this Agreement may, without the consent of Executive, be assigned by the Company to any person, firm, corporation or other business entity which at any time, whether by purchase, merger or otherwise, directly or indirectly, acquires all or substantially all of the assets or business of the Company or Parent. The Company will require any successor (whether direct or indirect, by purchase, merger or otherwise) to all or substantially all of the business or assets of the Company or Parent to assume this Agreement. Executive shall not be entitled to assign any of Executive's rights or obligations under this Agreement. This Agreement shall inure to the

benefit of and be enforceable by Executive's personal or legal representatives, executors, administrators, successors, heirs, distributees, devisees and legatees.

(b) Severability. In the event any provision of this Agreement is found to be unenforceable by a court of competent jurisdiction, such provision shall be deemed modified to the extent necessary to allow enforceability of the provision as so limited, it being intended that the parties shall receive the benefit contemplated herein to the fullest extent permitted by law. If a deemed modification is not satisfactory in the judgment of such court, the unenforceable provision shall be deemed deleted, and the validity and enforceability of the remaining provisions shall not be affected thereby.

(c) Interpretation; Waiver. The headings set forth in this Agreement are for convenience only and shall not be used in interpreting this Agreement. Either party's failure to enforce any provision of this Agreement shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Agreement.

(d) Governing Law and Venue. This Agreement will be governed by and construed in accordance with the laws of the United States and the State of New York applicable to contracts made and to be performed wholly within such State, and without regard to the conflicts of laws principles that would result in the application of the laws of another jurisdiction. Any suit brought hereon shall be brought in the state or federal courts sitting in New York, NY, the parties hereby waiving any claim or defense that such forum is not convenient or proper. Each party hereby agrees that any such court shall have in personam jurisdiction over it and consents to service of process in any manner authorized by New York law.

(e) Notices. Any notice required or permitted by this Agreement shall be in writing and shall be delivered as follows with notice deemed given as indicated: (i) by personal delivery when delivered personally; (ii) by overnight courier upon written verification of receipt; (iii) by telecopy or facsimile transmission upon acknowledgment of receipt of electronic transmission; or (iv) by certified or registered mail, return receipt requested, upon verification of receipt. Notice shall be sent to Executive at the most recent address for Executive set forth in the Company's personnel files and to the Company at its principal place of business, or such other address as either party may specify in writing.

(f) Survival. Sections 2 ("Severance"), 3 ("Condition to Severance Obligations"), 4 ("Agreement to Arbitrate") and 6 ("General Provisions") of this Agreement shall survive termination of Executive's employment with the Company.

(g) Entire Agreement. This Agreement and the Confidentiality and Restrictive Covenant Agreements incorporated herein by reference as set forth in Section 3 together constitute the entire agreement between the parties in respect of the subject matter contained herein and therein and supersede all prior or simultaneous representations, discussions, negotiations, and agreements, whether written or oral. This Agreement may be amended or modified only with the written consent of Executive and an authorized representative of the Company. No oral waiver, amendment or modification will be effective under any circumstances whatsoever.

(h) Trade Secrets; Whistleblower Protections. In accordance with 18 U.S.C. § 1833, notwithstanding anything to the contrary in this Agreement, the Confidentiality and Restrictive Covenant Agreements or any other agreement between Executive and the Company or any of its Affiliates (together, the "***Subject Documents***"): (i) Executive shall not be in breach of any Subject Document, and shall not be held criminally or civilly liable under any federal or state trade secret law (x) for the disclosure of a trade secret that is made in confidence to a federal, state, or local government official or to an attorney solely for the purpose of reporting or investigating a suspected violation of law, or (y) for the disclosure of a trade secret that is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is

made under seal; and (ii) if Executive files a lawsuit for retaliation by the Company for reporting a suspected violation of law, Executive may disclose the trade secret to Executive's attorney, and may use the trade secret information in the court proceeding, if Executive files any document containing the trade secret under seal, and does not disclose the trade secret, except pursuant to court order. Furthermore, nothing in any Subject Document prevents Executive from reporting possible violations of law or regulation to any governmental agency or entity in accordance with the provisions of and rules promulgated under Section 21F of the Exchange Act or Section 806 of the Sarbanes-Oxley Act of 2002, or any other whistleblower protection provisions of state or federal law or regulation (including the right to receive an award for information provided to any such government agencies).

(i) Code Section 409A.

(i) The intent of the parties is that the payments and benefits under this Agreement comply with or be exempt from Section 409A, and to the maximum extent permitted, this Agreement shall be interpreted in accordance with this intent.

(ii) Notwithstanding anything in this Agreement to the contrary, any compensation or benefits payable under this Agreement upon Executive's termination of employment shall be payable only upon Executive's "separation from service" with the Company within the meaning of Section 409A (a "***Separation from Service***"). If the period during which Executive may deliver the Release begins in one year and ends in the next, then to the extent required to comply with Section 409A, payments under Section 2 of this Agreement will in all events commence only in the later year.

(iii) Notwithstanding anything in this Agreement to the contrary, if Executive is deemed by the Company at the time of Executive's Separation from Service to be a "specified employee" for purposes of Section 409A, to the extent delayed commencement of any portion of the benefits to which Executive is entitled under this Agreement is required in order to avoid a prohibited distribution under Section 409A, such portion of Executive's benefits shall not be provided to Executive prior to the earlier of (i) the expiration of the six-month period measured from the date of Executive's Separation from Service with the Company or (ii) the date of Executive's death. Upon the first business day following the expiration of the applicable Section 409A period, all payments deferred pursuant to the preceding sentence shall be paid in a lump sum to Executive (or Executive's estate or beneficiaries), and any remaining payments due to Executive under this Agreement shall be paid as otherwise provided herein.

(iv) Executive's right to receive any installment payments under this Agreement shall be treated as a right to receive a series of separate payments and, accordingly, each such installment payment shall at all times be considered a separate and distinct payment as permitted under Section 409A. Except as otherwise permitted under Section 409A, no payment hereunder shall be accelerated or deferred unless such acceleration or deferral would not result in additional tax or interest pursuant to Section 409A.

(v) To the extent that any reimbursements under this Agreement are subject to Section 409A, any such reimbursements payable to Executive shall be paid to Executive no later than December 31 of the year following the year in which the expense was incurred, the amount of expenses reimbursed in one year shall not affect the amount eligible for reimbursement in any subsequent year, other than medical expenses referred to in Section 105(b) of the Code, and Executive's right to reimbursement under this Agreement will not be subject to liquidation or exchange for another benefit.

(j) Consultation with Legal and Financial Advisors. By executing this Agreement, Executive acknowledges that this Agreement confers significant legal rights, and may also involve the waiver of rights under other agreements; that the Company has encouraged Executive to consult with

Executive's personal legal and financial advisors; and that Executive has had adequate time to consult with Executive's advisors before executing this Agreement.

(k) Counterparts. This Agreement may be executed in multiple counterparts, each of which shall be deemed an original but all of which together shall constitute one and the same instrument. A facsimile, PDF, electronic signature or any other type of copy of an executed version of this Agreement signed by a party is binding upon the signing party to the same extent as the original of the signed Agreement.

(Signature Page Follows)

THE PARTIES TO THIS AGREEMENT HAVE READ THE FOREGOING AGREEMENT AND FULLY UNDERSTAND EACH AND EVERY PROVISION CONTAINED HEREIN. WHEREFORE, THE PARTIES HAVE EXECUTED THIS AGREEMENT AS OF THE DATE FIRST SET FORTH ABOVE .

[EMPLOYING SUBSIDIARY]

By: _____
Name: _____
Title: _____

EXECUTIVE

_____
[NAME]

EXHIBIT A

GENERAL RELEASE OF CLAIMS

[*The language in this Release may change based on legal developments and evolving best practices; this form is provided as an example of what will be included in the final Release document.*]

This General Release of Claims ("***Release***") is entered into between _____ ("***Executive***") and [EMPLOYING SUBSIDIARY] (the "***Company***") (collectively referred to herein as the "***Parties***"). Capitalized terms used but not defined in this Release shall have the meanings set forth in the Agreement (as defined below).

WHEREAS, Executive and the Company are parties to that certain Change in Control Agreement effective as of _____, ____ (the "***Agreement***");

WHEREAS, the Parties agree that Executive is entitled to certain severance benefits under the Agreement, subject to Executive's execution of this Release; and

WHEREAS, the Company and Executive now wish to fully and finally resolve all matters between them as set forth herein.

NOW, THEREFORE, in consideration of, and subject to, the severance benefits payable to Executive pursuant to the Agreement, the adequacy of which is hereby acknowledged by Executive, and which Executive acknowledges that he or she would not otherwise be entitled to receive, Executive and the Company hereby agree as follows:

1. General Release of Claims by Executive.

(a) Executive, on behalf of himself or herself and his or her executors, heirs, administrators, representatives and assigns, hereby agrees to release and forever discharge the Company and all predecessors, successors and their respective parent entities, affiliates, related, and/or subsidiary entities, including, without limitation, MeiraGTx Holdings plc ("***Parent***"), and all of their past and present investors, directors, shareholders, officers, general or limited partners, employees, attorneys, creditors, agents and representatives, and the employee benefit plans in which Executive is or has been a participant by virtue of his or her employment with or service to the Company (collectively, the "***Company Releasees***"), from any and all claims, debts, demands, accounts, judgments, rights, causes of action, equitable relief, damages, costs, charges, complaints, obligations, promises, agreements, controversies, suits, expenses, compensation, responsibility and liability of every kind and character whatsoever (including attorneys' fees and costs), whether in law or equity, known or unknown, asserted or unasserted, suspected or unsuspected, which Executive has or may have had against such entities based on any events or circumstances arising or occurring on or prior to the date Executive signs this Release, arising directly or indirectly out of, relating to, or in any other way involving in any manner whatsoever Executive's employment by or service to the Company or the termination thereof, including any and all claims arising under federal, state, or local laws relating to employment, including without limitation claims of wrongful discharge, breach of express or implied contract, fraud, misrepresentation, defamation, or liability in tort, and claims of any kind that may be brought in any court or administrative agency including, without limitation, claims under Title VII of the Civil Rights Act of 1964, as amended, 42 U.S.C. Section 2000, et seq.; the Americans with Disabilities Act, as amended, 42 U.S.C. § 12101 et seq.; the Rehabilitation Act of 1973, as amended, 29 U.S.C. § 701 et seq.; the Civil Rights Act of 1866, and the Civil Rights Act of 1991; 42 U.S.C. Section 1981, et seq.; the Age Discrimination in Employment Act, as amended, 29 U.S.C. Section 621, et seq. (the "***ADEA***"); the Equal Pay Act, as amended, 29 U.S.C. Section 206(d); regulations of the

Office of Federal Contract Compliance, 41 C.F.R. Section 60, et seq.; the Family and Medical Leave Act, as amended, 29 U.S.C. § 2601 et seq.; the Fair Labor Standards Act of 1938, as amended, 29 U.S.C. § 201 et seq.; the Employee Retirement Income Security Act, as amended, 29 U.S.C. § 1001 et seq.; and any similar state or local law.

Notwithstanding the generality of the foregoing, Executive does not release the following:

(i) Claims for unemployment compensation or any state disability insurance benefits pursuant to the terms of applicable state law;

(ii) Claims for workers' compensation insurance benefits under the terms of any worker's compensation insurance policy or fund of the Company;

(iii) Claims pursuant to the terms and conditions of the federal law known as COBRA;

(iv) Claims for indemnity under contract, the bylaws of the Company or its affiliates or any applicable insurance policy with respect to Executive's liability as an employee, director or officer of the Company or any of its affiliates pursuant to which Executive is covered as of the effective date of Executive's termination of employment with the Company;

(v) Claims for payment under Section 2(a) of the Agreement;

(vi) Executive's right to vested equity securities of Parent; and

(vii) Any rights that cannot be released as a matter of applicable law, but only to the extent such rights may not be released under such applicable law.

Further, this Release does not prevent Executive from reporting possible violations of federal law or regulation to any United States governmental agency or entity in accordance with the provisions of and rules promulgated under Section 21F of the Exchange Act or Section 806 of the Sarbanes-Oxley Act of 2002, or any other whistleblower protection provisions of state or federal law or regulation (including the right to receive an award for information provided to any such government agencies).

(b) Executive acknowledges that Executive is entitled to have [twenty-one (21)/forty-five (45)] days' time in which to consider this Release, and that such time period to review this Release shall not be extended upon any material or immaterial changes to this Release. Executive further acknowledges that the Company has advised Executive that Executive is waiving Executive's rights under the ADEA, and that Executive should consult with an attorney of Executive's choice before signing this Release, and Executive has had sufficient time to consider the terms of this Release. Executive represents and acknowledges that if Executive executes this Release before [twenty-one (21)/forty-five (45)] days have elapsed, Executive does so knowingly, voluntarily, and upon the advice and with the approval of Executive's legal counsel (if any), and that Executive voluntarily waives any remaining consideration period. Executive understands that nothing in this Release prevents or precludes Executive from challenging or seeking a determination in good faith of the validity of this waiver under the ADEA, nor does it impose any condition precedent, penalties, or costs for doing so, unless specifically authorized by federal law.

(c) Executive understands that after executing this Release, Executive has the right to revoke it within seven (7) days after Executive's execution of it. Executive understands that this Release will not become effective and enforceable unless the seven (7) day revocation period passes and Executive

does not revoke the Release in writing. Executive understands that this Release may not be revoked after the seven (7) day revocation period has passed. Executive also understands that any revocation of this Release must be made in writing and delivered to the Company at its principal place of business within the seven (7) day period.

(d) Executive understands that this Release shall become effective, irrevocable, and binding upon Executive on the eighth (8th) day after Executive's execution of it, so long as Executive has not revoked it within the time period and in the manner specified in clause (c) above. Executive further understands that Executive will not be given any severance benefits under the Agreement unless this Release is effective on or before the date that is 60 days following the date of Executive's termination of employment.

2. No Assignment. Executive represents and warrants to the Company Releasees that there has been no assignment or other transfer of any interest in any claim that Executive may have against the Company Releasees. Executive agrees to indemnify and hold harmless the Company Releasees from any liability, claims, demands, damages, costs, expenses and attorneys' fees incurred as a result of any such assignment or transfer from Executive.

3. Severability. In the event any provision of this Release is found to be unenforceable by an arbitrator or court of competent jurisdiction, such provision shall be deemed modified to the extent necessary to allow enforceability of the provision as so limited, it being intended that the parties shall receive the benefit contemplated herein to the fullest extent permitted by law. If a deemed modification is not satisfactory in the judgment of such arbitrator or court, the unenforceable provision shall be deemed deleted, and the validity and enforceability of the remaining provisions shall not be affected thereby.

4. Interpretation; Waiver. The headings set forth in this Release are for convenience only and shall not be used in interpreting this Agreement. Either party's failure to enforce any provision of this Release shall not in any way be construed as a waiver of any such provision, or prevent that party thereafter from enforcing each and every other provision of this Release.

5. Governing Law and Venue. This Release will be governed by and construed in accordance with the laws of the United States and the State of New York applicable to contracts made and to be performed wholly within such State, and without regard to the conflicts of laws principles that would result in the application of the laws of another jurisdiction. Any suit brought hereon shall be brought in the state or federal courts sitting in New York, NY, the parties hereby waiving any claim or defense that such forum is not convenient or proper. Each party hereby agrees that any such court shall have in personam jurisdiction over it and consents to service of process in any manner authorized by New York law.

6. Entire Agreement. This Release and the Agreement constitute the entire agreement of the Parties in respect of the subject matter contained herein and therein and supersede all prior or simultaneous representations, discussions, negotiations and agreements, whether written or oral. This Release may be amended or modified only with the written consent of Executive and an authorized representative of the Company. No oral waiver, amendment or modification will be effective under any circumstances whatsoever.

7. Counterparts. This Release may be executed in multiple counterparts, each of which shall be deemed to be an original but all of which together shall constitute one and the same instrument.

(Signature Page Follows)

IN WITNESS WHEREOF, and intending to be legally bound, the Parties have executed the foregoing Release as of the dates below.

[EMPLOYING SUBSIDIARY]

Dated: _____

By: _____
Name: _____
Title: _____

EXECUTIVE

Dated: _____

_____
[NAME]

Exhibit 21

SUBSIDIARIES OF MEIRAGTX HOLDINGS PLC

Legal Name of Subsidiary	**Jurisdiction of Organization**
BRI-Alzan, Inc.	Delaware
MeiraGTx B.V.	Netherlands
MeiraGTx Netherlands 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 Ireland DAC	Ireland
MeiraGTx Neurosciences, Inc.	Delaware
MeiraGTx Bio 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, 2021, 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, 2020.

/s/ Ernst & Young LLP

Stamford, Connecticut
March 11, 2021

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, 2020 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, 2021

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, 2020 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, 2021

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, 2020, 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, 2021

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, 2020, 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, 2021

By: /s/ Richard Giroux

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