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, 2024
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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		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. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

As of June 28, 2024, 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 $272,320,427 (based upon the closing sale price of the registrant's ordinary shares on that date on the Nasdaq Global Select Market).

As of March 9, 2025, the registrant had 78,854,936 ordinary shares outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2025 annual shareholder meeting to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2024 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, but not limited to, statements regarding our future results of operations and financial position, business strategy, financing, licensing and manufacturing arrangements, prospective products, development and timing of product candidates, timing of and expected success and efficacy of our product candidates, plans and objectives for future operations, expected future results of anticipated products and prospects, and 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.

- There is no guarantee that we will receive in a timely fashion or at all the additional milestone payments contemplated under the Asset Purchase Agreement or the revenues associated with our manufacture of the commercial supply of the RPGR Product under the Supply Agreement.

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

- We may not have sufficient cash flows or cash on hand to satisfy our debt obligations or covenants under our financing arrangements, or we may not be able to effectively manage our business in compliance with such covenants.

- Our review of potential strategic transactions may not result in an executed or consummated transaction or other strategic alternative and may not result in anticipated benefits to us or our shareholders, and the process of reviewing strategic transactions or its conclusion could be disruptive and distracting to our business operations and management.

- We are heavily dependent on the success of our product candidates, which are still in development, and if none of them receive regulatory approval or are successfully commercialized, our business may be harmed.

- It is difficult to predict the time and cost of product candidate development on our novel gene therapy platform. A limited number of 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 regulation and other legal obligations relating to data privacy and protection. Compliance with these requirements is complex and costly. The actual or perceived failure to comply with such obligations 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 may need to increase or decrease the size of our organization, and we may experience difficulties in managing these organizational changes, 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 genetic medicines company with a broad pipeline of late-stage clinical programs, including Parkinson's disease, radiation-induced xerostomia and AIPL1-associated retinal dystrophy. Our clinical programs use targeted local delivery of small doses of genetic medicines to treat both inherited and more common conditions with severe unmet need. The successful development of the clinical pipeline is supported by our internal end-to-end manufacturing capabilities. We have two viral vector production facilities for good manufacturing practices, or GMP, internal plasmid production for GMP, as well as an in-house Quality Control hub for stability and release, all fit for Investigational New Drug application (IND) through commercial supply. In addition, we have developed a proprietary manufacturing platform with leading yield and quality aspects and commercial readiness. Our core capabilities in viral vector and capsid optimization allow increased potency, decreased dose and significantly reduced cost of goods for our genetic medicines. We have developed a potentially transformative gene regulation platform using bespoke synthetic riboswitch technology invented in-house that allows for the precise, dose-responsive expression of any transgene under the control of oral small molecules. We are focusing the riboswitch platform on the *in vivo* delivery of biologic therapeutics such as the metabolic peptides glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic polypeptide (GIP), glucagon, amylin, peptide YY (PYY) and leptin via oral small molecules, as well as cell therapy for oncology and autoimmune diseases, and long term intractable pain. We have developed unique comprehensive technology capabilities to apply genetic medicine to more common diseases, increasing efficacy, addressing novel targets, and expanding access in some of the largest disease areas where the unmet need remains high.

We own and operate manufacturing facilities in London, United Kingdom and Shannon, Ireland that we expect can supply our current clinical and preclinical programs, as well as our third party supply obligations, 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 GMP, our 29,000 square foot flexible and scalable viral vector manufacturing facility in London, United Kingdom 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 GMP compliant manufacturing facility by the United Kingdom's Medicines and Healthcare products Regulatory Agency, or MHRA. The MHRA re-certified the facility in the second quarter of 2024.

Our second, large scale GMP viral vector manufacturing facility and our first GMP plasmid and DNA production facility in Shannon, Ireland, both of which are designed to meet GMP requirements, came online in 2022. The campus encompasses 150,000 square feet. It is the first commercial-scale gene therapy manufacturing site in Ireland and is unique in its scale and integrated capabilities. The site contains three facilities, one built to be flexible and scalable for viral vector production for clinical and commercial supply, in addition, a facility to manufacture plasmid DNA – the critical starting material for producing gene therapy products – and thirdly, a Quality Control (QC) hub performing advanced biochemical quality control testing for MeiraGTx clinical and commercial programs. In June 2023, we received a Manufacturer's/Importer's Authorization (MIA) for QC testing of commercial products in our GMP compliant manufacturing facility in Shannon from the Irish Health Products Regulatory Authority ("HRPA"). In September 2023, we received a second MIA from the HRPA for QC testing of investigational medicinal products. We believe that our second viral vector manufacturing facility and bringing GMP 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 designed for the efficient clinical development of the next generation of gene therapies and manufacturing in accordance with GMP requirements. We believe that our deep understanding of disease models informs our development of potency assays for the GMP production of our product

candidates, and our experienced teams 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. Our wholly-owned facilities have now produced GMP clinical trial material for eight different indications, using multiple AAV serotypes, including administration into the eye, salivary gland and central nervous system.

We have also developed a potentially transformative technology to precisely and specifically control gene expression levels via dose-response to orally delivered small molecules. This completely novel technology allows us to control the expression of any DNA sequence using a bespoke oral small molecule, circumventing the need for manufacturing of biologics outside the body or stabilization for long term activity. With this riboswitch platform, we can control the precise timing of production of any mRNA from any DNA sequence - and therefore regulate the protein or peptide produced within the body dependent on the dose of the chosen oral small molecule. The need for injection of stabilized drug product is replaced by an oral small molecule that can repeatedly activate mRNA production every time it is dosed. This platform opens a whole array of targets that are not currently druggable, particularly in the area of metabolism where many of the known peptide agonists have proven difficult to address pharmaceutically. We can deliver the sequence that is the most physiologically active without the need for modification to extend the half-life or manufacturing outside the body.

Relationship with Johnson & Johnson Innovative Medicine

On January 30, 2019, we and our wholly-owned subsidiary MeiraGTx UK II Limited entered into a Collaboration, Option and License Agreement with Johnson & Johnson Innovative Medicine (formerly known as Janssen Pharmaceuticals, Inc.), as further amended by that certain First Amendment to Collaboration, Option and License Agreement, dated as of December 16, 2021 (the "Collaboration Agreement"), for, among other things, the research, development and commercialization of gene therapies for the treatment of IRDs, including botaretigene sparoparvovec, or bota-vec (formerly referred to as AAV-RPGR), for the treatment of X-linked retinitis pigmentosa related to mutations in the retinitis pigmentosa GTPase regulator gene, or XLRP-RPGR (the "RPGR Product"), and two genetic forms of achromatopsia. Under the Collaboration Agreement, Johnson & Johnson Innovative Medicine paid us a non-refundable upfront fee of $100.0 million in March 2019 and a milestone payment of $30.0 million in December 2021. We also received funding for certain research, manufacturing, clinical development and commercialization costs, and had the opportunity to obtain potential additional milestone payments upon the achievement of such milestones and royalties on future net sales of products.

On December 20, 2023 (the "Closing Date"), we and MeiraGTx UK II Limited entered into and consummated an Asset Purchase Agreement (the "Asset Purchase Agreement") with Johnson & Johnson Innovative Medicine pursuant to which we sold and assigned to Johnson & Johnson Innovative Medicine, and Johnson & Johnson Innovative Medicine purchased and assumed, that certain License Agreement, dated February 5, 2019, by and between UCL Business Plc (now UCL Business Ltd.) ("UCLB"), on the one hand, and MeiraGTx UK II Limited and our wholly-owned subsidiary MeiraGTx Limited, on the other hand (the "UCLB RPGR License Agreement"), relating to the research, development, manufacture and exploitation of the RPGR Product, and other related assets as described in the Asset Purchase Agreement. In connection with entering into the Asset Purchase Agreement, we and MeiraGTx UK II Limited entered into a Termination Agreement with Johnson & Johnson Innovative Medicine on the Closing Date terminating the Collaboration Agreement.

MeiraGTx UK II Limited and Johnson & Johnson Innovative Medicine also entered into a Supply Agreement on the Closing Date pursuant to which MeiraGTx UK II Limited agreed to manufacture and supply the RPGR Product for Johnson & Johnson Innovative Medicine (the "Supply Agreement"). Under the Supply Agreement, MeiraGTx UK II Limited, together with its affiliates, will manufacture commercial supply of the RPGR Product for Johnson & Johnson Innovative Medicine for an initial term of four years, with Johnson & Johnson Innovative Medicine having an option to extend the Supply Agreement for a fifth year upon written notification to us.

Under the Asset Purchase Agreement, Johnson & Johnson Innovative Medicine paid us a non-refundable upfront cash purchase price of $65.0 million in December 2023. Additionally, pursuant to and subject to the terms and conditions set forth in the Asset Purchase Agreement, Johnson & Johnson Innovative Medicine agreed to pay us future contingent consideration of up to an aggregate of $350.0 million, as follows: (i) a milestone payment of $50.0 million in connection with the achievement of the initiation of the extension study for the Phase 3 LUMEOS clinical trial for the RPGR Product; (ii) $10.0 million upon completion of certain specified development services for the drug substance for the RPGR Product; (iii) $5.0 million upon completion of certain specified development services for the drug product for the RPGR Product; (iv) $175.0 million upon the first commercial sale of an RPGR Product in the United States; (v) $75.0 million upon the first commercial sale of an RPGR Product in at least one of the United Kingdom, France, Germany, Spain and Italy; (vi) $25.0 million upon completion of the transfer of certain manufacturing technology for drug substance and drug product from us to Johnson & Johnson Innovative Medicine; and (vii) $10.0 million upon regulatory approval of a Johnson & Johnson Innovative Medicine-selected manufacturing facility in each of the United States and European Union for commercial manufacture of the RPGR Product. As of December 31, 2024, we have received $60.0 million in milestone payments from Johnson & Johnson Innovative Medicine. Johnson & Johnson Innovative Medicine is also responsible for any royalty or milestone amounts that become payable on the RPGR Product under the UCLB RPGR License Agreement.

Strategic Investment from Sanofi

On October 30, 2023, we entered into an Investment Agreement (the "Investment Agreement") with Sanofi Foreign Participations B.V. (the "Sanofi Foreign Participations"), a wholly-owned subsidiary of Sanofi, and solely for the limited purposes set forth therein, Sanofi, pursuant to which, among other things and subject to the terms and conditions specified therein, we issued an aggregate of 4.0 million of our ordinary shares at a purchase price of $7.50 per share for gross proceeds of $30.0 million. The Investment Agreement also provides Sanofi Foreign Participations and its affiliates with a right of first negotiation for use of our riboswitch gene regulation technology for certain Immunology and Inflammation (I&I), including modulation of IL-4 and IL-13, and Central Nervous System (CNS) targets, as well as for GLP-1 and other gut peptides for metabolic disease, and for our Phase 2 xerostomia program, in each case, on the terms set forth therein.

Our Pipeline

Our focus is on *in vivo* delivery of vectorized biologic therapeutics addressing unmet needs in prevalent disorders, including severe forms of xerostomia, neurodegenerative diseases and ocular diseases, including inherited retinal diseases, or IRDs, as well as large degenerative ocular 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.

We are also focusing the riboswitch platform on delivery of metabolic peptides, as well as cell therapy for oncology and autoimmune diseases, and long term intractable pain.

A summary of our product candidates and the status of such product candidates as of March 1, 2025 is described below.

Product	Indication	Discovery / Preclinical	Phase 1/2	Phase 2	Phase 3
Salivary Gland					
AAV-AQP1	Xerostomia	*RMAT, Orphan Drug*		*Pivotal*	
	Sjögren's Syndrome				
Neurodegenerative Disease					
AAV-GAD	Parkinson's Disease				
AAV-UPF1	ALS				
BDNF for Genetic Obesity – MC4R					
BDNF- MC4R	Metabolic				
Riboswitch Inducible Expression Programs					
GLP-1-GIP Myokine combinations	Metabolic				
Ribo-CAR-T	Oncology				
Other prevalent indications	Undisclosed				
X-Linked RP					
Botaretigene sparoparvovec[1]	X-linked RP	*PRIME, Fast Track, Orphan Drug*			lumeos XLRP study
Inherited Retinal Diseases					
AAV-RPE65	RPE65-Associated Retinal Dystrophy	*RPDD, Orphan Drug*			
AAV-CNGB3	Achromatopsia	*RPDD, PRIME, Fast Track, Orphan Drug*			
AAV-CNGA3	Achromatopsia	*RPDD, Fast Track, Orphan Drug*			
AAV-AIPL1	LCA4	**RPDD, MHRA Specials License, Orphan Designation in US & EU**			
A007, A008	RDH12*, BBS10*, Stargardt, KCNV2	RPDD*			
Degenerative Ocular Diseases (non-inherited)					
	Wet & Dry AMD, Glaucoma, Uveitis				

[1] Remaining interests in program sold to Janssen in December 2023; MeiraGTx to receive up to an aggregate of $350.0 million upon achievement of milestones and will manufacture and supply commercial product for Janssen.

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:

- riboswitch gene regulation—use of our proprietary RNA shape regulation cassette to precisely control gene expression with novel small molecules, potentially transforming gene therapy technology into a delivery mechanism for a broad array of biologic drugs;

- 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; 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 Salivary Gland Programs

The clinical focus of our salivary gland program 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-hAQP1 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, resulting in a significant negative impact on patient quality of life. Current treatment options for RIX are few and are of limited benefit. The sialogogues pilocarpine (approved for RIX) and cevimeline (used off-label) are minimally effective in

patients with grade 2/3 RIX where the gland structure and function have been significantly impaired. No new medications for RIX have been approved in over 20 years.

Worldwide, there are approximately 650,000 new cases of head and neck cancer diagnosed each year, with approximately 54,000 cases in the U.S. 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 U.S., with approximately 15,000 new cases of persistent grade 2 or 3 RIX each year in the U.S. In addition to the RIX patient population from treatment for head and neck cancer, new therapies such as prostate specific membrane antigen (PSMA)-targeted radioligand therapy can also lead to xerostomia, providing additional potential patient populations that may benefit from our AAV-hAQP1 treatment.

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-hAQP1 to treat RIX by introducing a water conducting channel into the remaining epithelial cells of these damaged glands, thereby increasing water flow into the mouth. 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 resistant to ionizing radiation exposure. As a consequence of this relative resistance 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-hAQP1 introduces the gene for the human aquaporin water channel, or *hAQP1*. We have demonstrated that this has the potential to convey water permeability and cause ductal cells to generate an osmotic gradient, and secrete fluid into the lumen of the duct.

The proof of concept for this mechanism and its ability to increase the volume of fluid 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.

Clinical Development of AAV-hAQP1 for the Treatment of Radiation-Induced Grade 2/3 Xerostomia

We are currently conducting a Phase 1 dose escalation clinical trial of AAV-hAQP1 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. 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 an open-label, multi-center Phase 1 dose escalation clinical trial of a single administration of our product candidate AAV-hAQP1 to one or both parotid glands in patients with grade 2 or 3 RIX. In December 2021, we announced preliminary data from this Phase 1 clinical trial. The announcement included

data from seven patients treated in cohorts 1, 2 and 3 of the unilateral dose escalation phase of the clinical trial. Six of the seven patients who reached 90 days following treatment reported their symptoms of dry mouth as better following treatment pursuant to a validated patient reported assessment of xerostomia symptoms, constituting clinically meaningful improvement. One patient who reported the maximum response evaluable at 12-months had reached the 24-month time point and reported the same level of response. In March 2022, we completed enrollment of the study. A total of 24 patients received either unilateral (n=12) or bilateral (n=12) treatment in one of eight escalating dose cohorts of three patients each.

In June 2023, we announced additional positive clinical data from the completed Phase 1 dose escalation clinical trial of AAV-hAQP1. All unilaterally and bilaterally treated participants had undergone their 12-month assessment, with four having completed their 24-month assessment and three having completed their 36-month assessment in the long-term follow-up study. The investigational gene therapy AAV-hAQP1 was observed to be well tolerated in the Phase 1 trial, with no dose limiting toxicity or treatment-related serious adverse events observed, and patient reported assessments of xerostomia symptoms and whole salivary flow rate improved. All subjects are to be followed for one year post-treatment in the present study and for an additional four years in the long-term follow-up study, per U.S. Food and Drug Administration, or FDA, guidelines. The study's primary endpoint is safety. Secondary endpoints include change from baseline in patient reported measures of xerostomia symptoms as well as whole salivary flow rates. Based on the safety and efficacy data observed for AAV-hAQP1 in the Phase 1 clinical trial, we initiated in June 2023 a randomized, double-blind, placebo-controlled Phase 2 AQUAx2 study evaluating two active doses of AAV-hAQP1 for the treatment of grade 2 or 3 RIX with participants currently being enrolled and dosed in the U.S., Canada and UK. During 2024, we gained alignment with the FDA on requirements for the Phase 2 AQUAx2 clinical trial to be considered a pivotal trial in support of a potential Biologics License Application, or BLA, filing.

The FDA granted orphan drug designation to AAV-hAQP1 for the treatment of symptoms of grade 2 and grade 3 late xerostomia from parotid gland hypofunction caused by radiotherapy for cancer of the oral cavity. In December 2024, the FDA granted Regenerative Medicine Advanced Therapy, or RMAT, designation to AAV-hAQP1 for the treatment of grade 2 or 3 RIX.

AAV-hAQP1 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-hAQP1 vector. Supported by data from our preclinical studies and our ongoing RIX clinical trials, we are currently conducting IND-enabling studies of AAV-hAQP1 for xerostomia caused by Sjogren's syndrome.

Our Neurodegenerative Disease Programs

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 certain neurodegenerative diseases.

AAV-GAD for the Treatment of Parkinson's Disease

Our first target indication is Parkinson's disease, 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 via a one-time infusion through a minimally invasive procedure, using our proprietary device that allows infusion of the equivalent of one drop of gene therapy solution 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 filed an IND for AAV-GAD in May 2022, and we have completed dosing patients in MGT-GAD-025, an AAV-GAD Phase 1 bridging study. MGT-GAD-025 was a 6-month, three-arm, randomized, double-blind, sham-controlled study using AAV-GAD drug product manufactured at our wholly-owned facilities with our commercial platform process. Participants had idiopathic Parkinson's disease, a history of levodopa responsiveness for at least 12 months, and a UPDRS Part 3 score of ≥25 points in the "off" state. Fourteen subjects were randomized to one of three groups (high dose n=5, low dose n=5, and sham n=4). Subjects received either AAV-GAD infused bilaterally into the subthalamic nucleus or a sham procedure in a blinded fashion. The total dose per treated participant was 7.0×10^{10} vg (low dose group) or 21×10^{10} vg (high dose group). The primary objective of the study was to evaluate the safety and tolerability of AAV-GAD, with exploratory efficacy endpoints including the mean change from baseline to Week 26 in MDS-UPDRS Part 3 (motor examination) scores in the "off" state and the Parkinson's Disease Questionnaire (PDQ-39) score, a key patient-reported quality of life measure in Parkinson's disease. Subjects who completed this trial may enroll in a long-term follow-up study (NCT05894343), where they will be monitored for a total of five years post-treatment.

In October 2024, we announced preliminary data from this Phase 1 bridging study and the investigational gene therapy AAV-GAD was observed to be safe and well tolerated, with no treatment-related serious adverse events observed. At Week 26, a statistically significant 18-point average improvement from baseline in UPDRS Part 3 "off" medication score was demonstrated in the high dose group (p=0.03), with no significant change in the sham or low dose groups. A change of 5 to 10 points is considered clinically meaningful for the UPDRS Part 3 in the "off" state. Significant improvements from baseline in the disease-specific, patient-reported quality of life PDQ-39 score were demonstrated in both the high and low dose groups with no significant change in the sham group at Week 26:

- In the high dose AAV-GAD group, the PDQ-39 score improved by 8 points from baseline (p=0.02), the low dose group improved by 6 points from baseline (p=0.04), while the 0.2 point worsening in the sham surgery group was not statistically significant. For the PDQ-39, a 2 to 4-point change is considered clinically meaningful.

- A dose response in PDQ-39 score was observed, with 100% of participants in the high dose group, 60% of participants in the low dose group, and 25% of participants in the sham surgery group reporting an improvement.

- For the PDQ-39 score, there was a trend to significance between the high dose and sham surgery groups at 6 months (n=4 evaluable per group).

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 amyotrophic lateral sclerosis (ALS), and an Alzheimer's disease program focused on endosomal trafficking dysfunction. Each of these programs is 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 has 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 Ophthalmology Programs

Under our ophthalmology programs, we aim to provide treatments for eye diseases with durable, long-term clinical benefit that will halt vision loss in patients. We have three 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* genes, respectively, and AAV-RPE65 for retinal dystrophy related to mutations in the *RPE65* gene, or RPE65 deficiency. We have completed enrollment and dosing in all three of these programs. In addition to these three programs, AAV-AIPL1 has been 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 the *AIPL1* gene. We also 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, Bardet-Biedl syndrome, or BBS, due to *BBS10* mutations, Leber congenital amaurosis type 1, or LCA1, due to *GUCY2D* mutations and Stargardt disease related to mutations in the *ABCA4* gene.

We chose diseases of the eye as an 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 was 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.

We believe that 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 GMP manufacturing.

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 (U.S.) 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 retinitis pigmentosa, or 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 Germany, France, Spain, Italy and the UK, 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 conducted a natural history study in patients with RPE65-associated retinal dystrophy with approximately 30 patients enrolled that has allowed 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 continue to evaluate the initiation of a Phase 3 clinical trial for AAV-RPE65.

The FDA granted orphan drug designation and the European Commission (based on the European Medicines Agency's, or EMA, opinion) granted orphan designation to AAV-RPE65 for the treatment of LCA caused by mutations in the *RPE65* gene. 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, Germany, France, Spain, Italy and the UK, 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 also conducted a natural history study in ACHM including over 90 patients that allows us to collect structural and functional data on prospectively defined endpoints, including functional tests, retinal imaging and electrophysiological assessments. We believe access to these ACHM patients 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 allowed 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 the CNGB3 Gene

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 have completed enrollment and dosing of the 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 could participate in a long term follow up study in which they were followed for safety and indication of benefit.

Our gene therapy product candidate AAV-CNGB3 was granted orphan drug designation by the FDA and orphan designation by the European Commission for the treatment of achromatopsia caused by mutations in the *CNGB3* gene, 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 the CNGA3 Gene

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 have completed enrollment and dosing of the open-label, dose-escalation Phase 1/2 clinical trial of AAV-CNGA3 in patients with ACHM due to mutations in the *CNGA3* gene. Six months following treatment, patients could participate in a long term follow up study in which they were followed for safety and indication of benefit.

Our gene therapy product candidate AAV-CNGA3 was granted orphan drug designation by the FDA and orphan designation by the European Commission, rare pediatric disease designation by the FDA, and was granted Fast Track designation by the FDA for the treatment of ACHM caused by *CNGA3* mutations.

AAV-AIPL1 for the Treatment of LCA4

LCA4 is an IRD that causes profound visual impairment from birth, with all children being legally blind (often light perception only) from birth. Despite the severe lack of retinal function, there is a narrow window of relative preservation of central retinal structure until four years of age. Aryl-hydrocarbon-interacting protein-like 1, or AIPL1, is a key protein for the maintenance of photoreceptor structure and function. LCA4 is rare, representing approximately 5% 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. In research published in the March 2024 issue of *Molecular Therapy Nucleic Acids*, AAV-AIPL1 was reported to have effectively rescued molecular features of AIPL1-associated LCA4 in a study involving LCA4 patient-derived retinal organoids.

LCA4's extremely rapid progression (e.g., no targetable central retina beyond four years of age), rarity and early age of onset all 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.

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 11 children with LCA4. A specials license allows physicians to prescribe a treatment of AAV-AIPL1 for patients with LCA4 that they deem appropriate with local ethics approval. We play no role in the physician's treatment decision. The results from the first-in-human interventional study to treat children with AIPL1-associated retinal dystrophy were published in *The Lancet* in February 2025, which study sought to evaluate whether early intervention by gene supplementation therapy was safe and could improve outcomes in young children with this condition. The findings indicate that children under the age of 4 years old with AIPL1-related retinal dystrophy benefited substantially from subretinal administration of rAAV8.hRKp.AIPL1, with improved visual acuity and functional vision and evidence of protection against progressive retinal degeneration, without serious adverse effects.

The non-randomized, single-arm, clinical study conducted in the UK involved four children aged one year to three years with severe retinal dystrophy associated with biallelic disease-causing sequence variants in AIPL1. The genetic medicine was a recombinant adeno-associated viral vector, comprising the human AIPL1 coding sequence driven by a human rhodopsin kinase promoter region (rAAV8.hRKp.AIPL1). The product candidate was administered to one eye of each child by subretinal injection. Outcome measures included visual acuity (as assessed with standard-of-care testing as well as a novel touchscreen test), functional vision (assessed by observing and recording the children's visual behavior and their ability to perform simple vision-guided tasks), visual evoked potentials (assessed by recording cortical electrophysiological responses to full-screen black-and-white flickering stimuli), and retinal structure (assessed with handheld OCT and widefield fundus imaging).

Prior to intervention, the children's binocular visual acuities, or VA, were limited to perception of light. At a mean of 3.5 years (range 3.0 to 4.1 years), after intervention the VAs of their treated eyes improved to a mean of 0.9 logarithm of the minimal angle of the minimum angle of resolution (LogMAR) (range 0.8 to 1.0); VAs before intervention were equivalent to 2.7 LogMAR. In contrast, the VAs of their untreated eyes became unmeasurable at the final follow-up. In the 2 children able to comply with testing, an objective test of VA confirmed improvements in visual function, and measurement of visual evoked potentials showed enhanced activity of the visual cortex, specific to the treated eyes. In 3 of the children, structural lamination of the outer retina was better preserved in the treated eye than in the untreated eye, and, for all 4 children, retinal thickness appeared better preserved in the treated eye than in the untreated eye.

To date, two cohorts of children have been treated with rAAV8.hRKp.AIPL1. The first cohort of 4 children (data published in *The Lancet*) received treatment in one eye. A second cohort has been treated, with 7 children (ages 1 to 3 years old) receiving sequential bilateral treatment. Meaningful responses have been observed in all 11 out of 11 LCA4 children treated with rAAV8.hRKp.AIPL1 to date, with all gaining visual acuity 4 or more weeks following treatment.

Following recent meetings with the MHRA, we intend to submit a marketing authorization application, or MAA, under exceptional circumstances for AAV-AIPL1 in the UK based on the results from the 11 treated children. We are also currently engaging with the FDA to discuss a path forward for regulatory approval in the U.S.

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 (as amended) 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.

We were awarded an Innovation Passport Designation by the U.K. Innovative Licensing and Access Pathway Steering Group for AAV8-RK-AIPL1. This designation provides entry into the U.K.'s Innovative Licensing and Access Pathway, or ILAP, designed to accelerate time to market and patient access to innovative medicines. Other benefits of ILAP include access to a range of development tools, such as the potential for accelerated MAA assessment, rolling review, and a continuous benefit-risk assessment, or potential marketing authorization under exceptional circumstances.

Our gene therapy candidate AAV-AIPL1 was granted orphan drug designation by the FDA and orphan designation by the European Commission for treatment of inherited retinal dystrophy due to defects in the *AIPL1* gene, and in November 2024, rare pediatric disease designation by the FDA for treatment of inherited retinal dystrophy due to defects in the *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 received orphan drug designation from the FDA and orphan designation from the European Commission, and in November 2024, rare pediatric disease designation from the FDA, for AAV-RDH12 for the treatment of RDH12-associated retinal dystrophy.

AAV-BBS10 for the Treatment of BBS due to BBS10 Mutations

BBS is a rare genetic disease affecting approximately 1 in 250,000 people around the world. One of the primary symptoms of BBS is visual impairment secondary to retinal degeneration. More than 20 different genes are associated with the development of BBS, with BBS10 accounting for approximately 25% of cases. Our investigational genetic medicine AAV-BBS10 is an adeno-associated virus with a serotype 8 capsid with a complementary DNA (cDNA)

encoding the human BBS10 gene for treatment of BBS due to *BBS10* mutations. In November 2024, the FDA granted rare pediatric disease designation to AAV-BBS10 for the treatment of BBS due to *BBS10* mutations.

AAV-RetGC for the Treatment of LCA1

Mutations in the GUCY2D gene coding for guanylate cyclase lead to severe retinal diseases in humans, with 88% of cases causing autosomal recessive LCA1 whilst heterozygous missense mutations cause autosomal dominant cone-rod dystrophy, or CRD. In LCA1, photoreceptor function loss and blindness emerge very early in life. In CRD, degeneration starts in the cones and leads to loss of the central visual field due to the high presence of cones in the macula. CRD can lead to complete blindness when degeneration of rods follows those of cones. In January 2025, the FDA granted rare pediatric disease designation to AAV-RetGC for the treatment of LCA1 due to *GUCY2D* mutations.

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 candidate 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 designed 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 Strengths

In addition to our three core therapeutic areas of focus, our 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 platform using bespoke synthetic riboswitch technology invented in-house that allows for the precise, dose-responsive expression of any transgene under the control of oral small molecules. 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 GMP manufacturing and clinical development through commercialization.

- **Potentially Transformative Gene Regulation Platform Technology:** We have developed a proprietary riboswitch technology platform to enable us to control the expression of any DNA sequence in the body using a bespoke oral small molecule, circumventing the need for manufacturing of biologics outside the body or stabilization for long term activity. We believe the capacity for temporal control of gene expression has the potential to transform the way gene and cell therapy can be used, including opening a whole array of targets that are not currently druggable, particularly in the area of metabolism where many of the known peptide agonists have proven difficult to address pharmaceutically.

- **Manufacturing Capabilities and Capacity:** We have manufacturing facilities in London, United Kingdom and Shannon, Ireland, which we expect can supply our current clinical and preclinical programs, as well as our third party supply obligations, through regulatory approval and, should they be approved, provide sufficient capacity for their commercial production. Our 29,000 square foot flexible and scalable viral vector manufacturing facility in London 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. Our second, large scale GMP viral vector manufacturing facility and our first GMP plasmid and DNA production facility in Shannon, Ireland came online in 2022 and stretches over 150,000 square feet. It is the first commercial-scale gene therapy manufacturing site in Ireland and is unique in its scale and integrated capabilities. The site contains three facilities, one built to be flexible and scalable for viral vector production for clinical and commercial supply, in addition, a facility to manufacture plasmid DNA – the critical starting material for producing gene therapy products – and thirdly, a QC hub performing advanced biochemical quality control testing for our clinical and commercial programs.

- **Robust and Diverse Clinical and Preclinical Pipeline:** Applying our portfolio approach to gene therapy product development, our focus is on *in vivo* delivery of vectorized biologic therapetuics addressing unmet needs in prevalent disorders, including treatments for ocular disorders, including IRDs and large degenerative ocular diseases, as well as salivary gland disorders and neurodegenerative diseases. We also have 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 clinical studies to support potential 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.

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 55 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, more than 40 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 Gene Regulation Platform

We have developed a potentially transformative technology designed to precisely and specifically control gene therapy expression levels via dose-response to orally delivered small molecules. 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 or peptide would be delivered to target cells in the body, but these transgenes would only be activated in the presence of a specific, proprietary small molecule. The therapeutic protein would be manufactured by the patient's 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 expression 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 field 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.

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, and demonstrated the ability to switch genes on and off in mammalian cells and *in vivo* in mice and non-human primates. 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 unprecedented dynamic range of greater than 5,000-fold. 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 demonstrated the ability to regulate multiple genes *in vitro* and *in vivo* in multiple tissue types using multiple small molecules.

Using this technology *in vivo*, we have delivered ongoing efficacious levels of multiple therapeutic antibodies with a daily small molecule dose.

We have also delivered peptides and growth factors such as erythropoietin (EPO), human growth hormone (hGH), and parathyroid hormone (PTH) - rescuing hematocrit, little mouse growth or calcium to physiological levels, respectively, with daily oral dosing of our small molecule. In addition, we have now delivered combinations of gut peptides such as GLP-1, GIP glucagon, amylin, PYY and leptin, and we have shown that the efficacy with respect to glucose control is better than constitutively active expression of those peptides.

In cell therapy, we can control any chimeric antigen receptor (CAR) or receptor or cell fate determining factor to a specific level at a specific time, thus allowing us to precisely control the cell fate of transplanted cells. We can knock our regulation mechanism into T-cells to regulate CAR expression in CAR-T, and have demonstrated reduced exhaustion, improved T-cell profile, improved cytotoxicity, and 3-4x increased potency in tumor killing, *in vivo*, compared to existing CAR-T therapies.

For gene editing nucleases, we can very tightly regulate nuclease expression from 0% to close to 100% activity using our small molecules, allowing transient expression of DNA editors to achieve efficient editing, avoiding undesirable constitutive expression of the nuclease.

The riboswitch platform provides the ability to express any mRNA and therefore any protein or peptide in the body on an ongoing basis via the dosing of an oral pill. We are now applying this to metabolic peptides that are agonists

of muscle metabolism and fat browning – which are not readily made sufficiently stable to be injectable recombinant drugs. This opens an entire array of targets that are not currently druggable, particularly in the area of metabolism where many of the known peptide agonists have proven difficult to address pharmaceutically. We express the natural peptide sequence that is the most physiologically active, without the need for modification to extend the half-life, or manufacturing outside the body.

In October 2023, we announced that under the terms of the Investment Agreement we entered into with Sanofi and Sanofi Foreign Participations, Sanofi has a right of first negotiation for use of our riboswitch gene regulation technology for certain Immunology and Inflammation (I&I), including modulation of IL-4 and IL-13, and Central Nervous System (CNS) targets, as well as for GLP-1 and other gut peptides for metabolic disease, and for our Phase 2 xerostomia program.

Our Manufacturing Capabilities

We own and operate a GMP 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.

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.

Our second, large scale GMP viral vector manufacturing facility and our first GMP plasmid and DNA production facility in Shannon, Ireland came online in 2022. The campus encompasses 150,000 square feet and contains three facilities, one built to be flexible and scalable for viral vector production for clinical and commercial supply, in addition, a facility to manufacture plasmid DNA – the critical starting material for producing gene therapy products – and thirdly, a QC hub performing advanced biochemical quality control testing for MeiraGTx clinical and commercial programs.

We believe that building a second viral vector manufacturing facility and bringing GMP plasmid and DNA production, as well as QC analytics, in-house provides greater flexibility and efficiency as we advance our product candidates through development, and should they be approved, commercial production.

We have more than 200 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 believe our facilities can supply our current clinical and preclinical programs, as well as our third party supply obligations, through regulatory approval and, should they be approved, provide sufficient capacity for commercial production. Strategically, we believe our facilities will minimize our dependence on third-party contract manufacturers, which we believe provides a significant strategic, clinical and commercial advantage, as well as significantly reduce the cost of goods sold for our programs.

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.

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 Luxturna, marketed by Spark Therapeutics, Inc., which 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. and Eli Lilly and Company.

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 comprises a combination of issued patents and pending patent applications that are owned or licensed from third parties. In addition, we also evaluate opportunities to sublicense our portfolio of patents and patent applications that we own or exclusively license, and we may enter into such licenses from time to time.

As of December 31, 2024, we own, co-own, or have an exclusive license to 661 United States and foreign issued or allowed patents and 533 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 eight patent families relating to gene regulation platform technologies developed by us with a combined 187 United States and foreign issued patents and 129 pending patent applications.

The first patent family includes 58 issued patents in the United States (two patents), African Regional Intellectual Property Organization, Albania, Australia (two patents), Austria, Belgium, Bulgaria, China, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Eurasian Patent Organization, Finland, France, Germany, Greece, Hong Kong, Hungary, Iceland, India, Ireland, Israel (two patents), Italy, Japan (two patents), Republic of Korea, Latvia, Lithuania, Luxembourg, Malaysia, Malta, Mexico, Monaco, Netherlands, New Zealand, North Macedonia, Norway, Philippines, Poland, Portugal, Romania, San Marino, Serbia, Singapore, Slovakia, Slovenia, South Africa (two patents) Spain, Sweden, Switzerland/Liechtenstein, Turkey and the United Kingdom and 20 pending patent applications with claims directed to compositions of matter and methods of use in the United States, African Regional Intellectual Property Organization, Australia, Brazil, Canada, China, Egypt, Eurasian Patent Organization, European Patent Organization, Hong Kong (two applications), Indonesia, Japan, Republic of Korea, Mexico, New Zealand, Philippines, Singapore, South Africa and Vietnam. 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 48 issued patents in the United States, Albania, Australia, Austria, Belgium, Bulgaria, China, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hong Kong, Hungary, Iceland, India, Indonesia, Ireland, Israel, Italy, Japan, Latvia, Lithuania, Luxembourg, Malaysia, Malta, Mexico, Monaco, Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, San Marino, Serbia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland/Liechtenstein, Turkey and the United Kingdom and 15 pending patent applications with claims directed to compositions of matter and methods of use in the United States, African Regional Intellectual Property Organization, Brazil, Canada, Egypt, Eurasian Patent Organization, India, Indonesia, Republic of Korea, New Zealand, Philippines (two applications), South Africa and Vietnam (two applications). 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 11 issued patents in the United States, African Regional Intellectual Property Organization, Australia, China, Eurasian Patent Organization, India, Indonesia, Japan, Malaysia, Mexico and Singapore and 12 pending patent applications with claims directed to compositions of matter and methods of use in the United States, Brazil, Canada, Egypt, European Patent Organization, Hong Kong, Israel, Republic of Korea, New Zealand, Philippines, South Africa and Vietnam. 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 51 issued patents in the United States, Albania, Australia, Austria, Belgium, Bulgaria, Canada, China, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Eurasian Patent Organization, Finland, France, Germany, Greece, Hong Kong, Hungary, Iceland, India, Indonesia, Ireland, Israel, Italy, Japan, Republic of Korea, Latvia, Lithuania, Luxembourg, Malta, Malaysia, Mexico, Monaco, Netherlands, New Zealand, North Macedonia, Norway, Poland, Portugal, Romania, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland/Liechtenstein, Turkey and the United Kingdom and 10 pending patent applications with claims directed to compositions of matter and methods of use in the United States, African Regional Industrial Property Organization, Australia, Brazil, Egypt, New Zealand, Philippines, Singapore, South Africa and Vietnam. 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 nine issued patents in the United States, African Regional Industrial Property Organization, Australia, China, Indonesia, Japan, Republic of Korea, Mexico and Philippines, and 16 pending patent applications with claims directed to compositions of matter and methods of use in the United States, Australia, Brazil, Canada, Egypt, Eurasian Patent Organization, European Patent Organization, Hong Kong, India, Israel, Malaysia, New Zealand (two applications), Singapore, South Africa and Vietnam. 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 nine issued patents in African Regional Industrial Property Organization, China, Indonesia, Israel, Japan, Republic of Korea, Malaysia, Mexico and New Zealand and 14 pending patent applications with claims directed to compositions of matter and methods of use in the United States, Australia, Brazil, Canada, Egypt, Eurasian Patent Organization, European Patent Organization, Hong Kong, India, New Zealand, Philippines, Singapore, South Africa and Vietnam. 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.

The seventh patent family includes one issued patent in Japan and 21 pending patent applications with claims directed to compositions of matter and methods of use in the United States, African Regional Industrial Property Organization, Australia, Brazil, Canada, China, Egypt, Eurasian Patent Organization, European Patent Organization, Hong Kong, India, Indonesia, Israel, Republic of Korea, Malaysia, Mexico, New Zealand, Philippines, Singapore, South Africa and Vietnam. Patents issued from this family are expected to expire on March 24, 2041, not including any patent term adjustments that may extend the patent term in certain jurisdictions.

The eighth patent family includes 21 pending applications with claims directed to compositions of matter and methods of use in the United States of America, African Regional Industrial Property Organization, Australia, Brazil, Canada, China, Egypt, Eurasian Patent Organization, European Patent Convention, India, Indonesia, Israel, Japan, Republic of Korea, Malaysia, Mexico, New Zealand, Philippines, Singapore, South Africa, and Vietnam. Patents issued from this family are expected to expire on December 15, 2042, not including any patent term adjustments that may extend the patent term in certain jurisdictions.

Licensed Intellectual Property

Certain of our issued patents and pending patent applications are exclusively licensed to us from UCLB, Brandeis University ("Brandeis") and the National Institute of Dental and Craniofacial Research ("NIDCR").

UCLB

The UCLB portfolio includes two licensed patent families relating to our *RPE65*, *CNGA3* and dry AMD gene therapy programs with a combined 150 United States and foreign issued patents and 30 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 52 issued patents in the United States (two patents), Albania, Australia, Austria, Belgium, Bulgaria, Canada, China, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hong Kong, Hungary, Iceland, India, Ireland, Israel (two patents), Italy, Japan, Latvia, Lithuania, Luxembourg, Malta, Malaysia, Mexico, Monaco, Netherlands, New Zealand, North Macedonia, Norway, Philippines, Poland, Portugal, Romania, San Morino, Serbia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland/Liechtenstein, Turkey and the United Kingdom and 7 pending patent applications in the United States, Brazil, European Patent Organization, Hong Kong, Mexico, Nigeria 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 44 issued patents in the United States, African Regional Intellectual Property Organization, Albania, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Eurasian Patent Convention, Finland, France, Germany, Greece, Hungary, Iceland, Indonesia, Ireland, Italy, Japan, Latvia, Lithuania, Luxembourg, Malta, Monaco, Netherlands, New Zealand, North Macedonia, Norway, Poland, Portugal, Romania, San Marino, Serbia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland/Liechtenstein, Turkey and United Kingdom and 16 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, Australia, Brazil, Canada, China, Egypt, Hong Kong, India, Israel, Republic of Korea, Malaysia, Mexico, New Zealand, Philippines, South Africa and Vietnam. 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 dry AMD gene therapy program, includes 54 issued patents in African Regional Intellectual Property Organization, Albania, Austria, Australia (two patents), Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Eurasian Patent Organization, Finland, France, Germany, Greece, Hong, Kong, Hungary, Iceland, Indonesia, Ireland, Israel, Italy, Japan, Republic of Korea, Latvia, Lithuania, Luxembourg, Malta, Malaysia, Mexico, Monaco, Netherlands, New Zealand, Nigeria, North Macedonia, Norway, Poland, Portugal, Romania, San Marino, Serbia, Singapore (two patents), Slovakia, Slovenia, Spain, South Africa, Sweden, Switzerland/Liechtenstein, Turkey and the United Kingdom and seven pending applications in the United States, Brazil, China, Hong Kong, Philippines, Thailand and Vietnam. 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.

On December 20, 2023, we and MeiraGTx UK II Limited sold and assigned to Johnson & Johnson Innovative Medicine the rights to a fourth patent family related to the RPGR Product, which had been previously licensed from UCLB.

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 17 issued patents in the United States (two patents), Austria, Australia, Belgium, Denmark, France, Germany, Hong Kong, Ireland, Italy, Netherlands, Norway, Spain, Sweden, Switzerland/Liechtenstein and the United Kingdom and 4 pending patent applications in the United States, Canada European Patent Organization and Hong Kong. Patents issued from this family are expected to expire October 8, 2033, not including any patent term extensions or adjustments that may extend the patent term in certain jurisdictions.

NIDCR

The exclusively licensed NIDCR portfolio includes two patent families.

The first patent family has 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, Australia, Austria, Belgium, Canada, Denmark, France, Germany, Ireland, Italy, Netherlands, Norway, Spain, Sweden, Switzerland/Liechtenstein 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.

The second patent family has claims directed to methods of use for our radiation-induced salivary dysfunction gene therapy program. This patent family includes 18 pending applications in the United States of America, African Regional Industrial Property Organization, Australia, Brazil, Canada, China, Eurasian Patent Organization, European Patent Convention, Hong Kong, Israel, Japan, Republic of Korea, Malaysia, Mexico, New Zealand, Philippines, Singapore, and South Africa. Patents issued from this family are expected to expire August 4, 2042, 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 caused by mutations in RPGR; 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 UCLB 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 UCLB 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 UCLB 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.

The First UCLB License Agreement had also included an option to the dry AMD gene therapy program. This option was exercised under a separate license agreement dated March 23, 2020.

As noted above, on December 20, 2023, we and MeiraGTx UK II Limited entered into and consummated an Asset Purchase Agreement with Johnson & Johnson Innovative Medicine pursuant to which we sold and assigned to Johnson & Johnson Innovative Medicine, and Johnson & Johnson Innovative Medicine purchased and assumed, the UCLB RPGR License Agreement relating to the research, development, manufacture and exploitation of the RPGR Product, and other related assets as described in the Asset Purchase Agreement. Johnson & Johnson Innovative Medicine is responsible for any royalty or milestone amounts that become payable on the RPGR Product under the UCLB RPGR License Agreement.

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 $4.5 million. 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 is the subject of registrations and/or pending applications in the U.S., UK and EU.

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 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 BLA process before they may be legally marketed in the United States. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

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

- submission to the FDA of an IND 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;

- preparation and 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;

- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with current GMP, or 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;

- FDA review and approval, or licensure, of the BLA prior to any commercial marketing or sale of the product in the United States; and

- compliance with any post-approval requirements, including the potential requirement to conduct post-approval studies.

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 certain preclinical tests must comply with certain 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 GMP and cGMP requirements, as applicable. 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.

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 must

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. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan drug 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 drug 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 drug 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 disease or condition 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 drug-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 disease or condition 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 product candidates that meet certain criteria. Specifically, biological product candidates 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 candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the review team during product development and, once a BLA is submitted, the application may be eligible for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the BLA 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.

In addition, the FDA established a Breakthrough Therapy designation which is intended to expedite the development and review of products that are intended to treat serious or life-threatening diseases or conditions. A Breakthrough Therapy-designated product candidate is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product 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.

Any product candidate submitted to the FDA for marketing, including a product that has received a Fast Track or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. 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 potential for 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. Priority review means the FDA's goal is to take action on an application within six months (compared to 10 months under standard review).

Additionally, product candidates 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 upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on a clinical endpoint that can be measured earlier than the irreversible morbidity or mortality that is reasonably likely to predict an effect on 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 accelerated approval, the FDA will generally require that the sponsor perform adequate and well-controlled confirmatory clinical trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit, and may require that such confirmatory trials are underway prior to granting any accelerated approvals. Failure to conduct required confirmatory trials in a timely manner, 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.

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 these designations are received, the FDA may later decide that a product candidate no longer meets the conditions for qualification.

Rare Pediatric Disease Designation and Priority Review Vouchers

Under the FDCA, as amended, the FDA incentivizes the development of drugs and biologics for the prevention and treatment of rare pediatric diseases. A "rare pediatric disease" is defined to include a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged 18 years of age or younger and the disease affects fewer than 200,000 individuals in the U.S., or affects more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for such disease or condition will be recovered from sales in the U.S. of such drug. The sponsor of a product candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a subsequent human drug application after the date of approval of the rare pediatric disease drug product, referred to as a priority review voucher. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its BLA. A rare pediatric disease designation does not guarantee that a sponsor will receive a priority review voucher upon approval of its BLA. If a priority review voucher is received, it may be sold or transferred an unlimited number of times. The FDA's rare pediatric disease priority voucher program began to sunset on December 20, 2024, after Congress failed to pass a continuing resolution package that included its reauthorization. Under the amended statutory sunset provisions, after December 20, 2024, the FDA may award a priority review voucher for an approved rare pediatric disease product application only if the sponsor has rare pediatric disease designation for the drug and if that designation was granted by December 20, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers. Congress may vote to reauthorize this program, but its future remains unknown at this time.

Post-Approval Requirements

Once a BLA is approved, a product will be subject to rigorous and extensive FDA regulation including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, adverse event reporting and advertising, manufacturing, and marketing and promotion. Biological products may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. While physicians may prescribe a product for uses in patient populations that are not described in the product's approved labeling, or "off-label" uses, manufacturers may only promote a product for the approved indications and in accordance with the provisions of the approved label of such product. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of "off-label" uses, and a company that is found to have improperly promoted "off-label" uses may be subject to significant liability.

After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which the FDA assesses an annual program fee for each product identified in an approved BLA. Manufacturers are also 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. 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 and transparency laws and regulations regarding drug pricing and payments or other transfers of value made to physicians and other licensed healthcare professionals. 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 healthcare 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 contained 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 healthcare programs.

Since its enactment, there have been judicial, Congressional and executive branch challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers, which was temporarily suspended from May 1, 2020 through March 31, 2022, and reduced payments to several types of Medicare providers. In March 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminated the statutory Medicaid drug rebate cap for single source and innovator multiple source drugs, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

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. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new manufacturer discounting program (which began in 2025). The IRA permits the Secretary of the Department of Health and Human Services, or HHS, to implement many of these provisions through guidance, as opposed to regulation, for the initial years. The Centers for Medicare & Medicaid Services, or CMS, has published the negotiated prices for the initial ten drugs, which will first be effective in 2026, and the list of the subsequent 15 drugs that will be subject to negotiation, although the Medicare drug price negotiation program is currently subject to legal challenges. While the impact of the IRA on the pharmaceutical industry cannot yet be fully determined, it is likely to be significant. 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, drug price reporting and other transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Some states have enacted legislation creating so-called prescription drug affordability boards, which ultimately may attempt to impose price limits on certain drugs in these states.

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 Laws

In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws, including the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations promulgated thereunder, or collectively, HIPAA, and federal and state and consumer protection laws and regulations (e.g., Section 5 of the Federal Trade Commission Act), 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. In addition, certain state laws, such as the California Consumer Privacy Act, as amended by the California Privacy Rights Act, or collectively, the CCPA, 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 make compliance efforts more challenging, and can result in investigations, proceedings, or actions that lead to significant 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 may be subject to a variety of regulations in other jurisdictions, for instance in the UK or EU, governing, among other things, clinical trials, marketing authorizations, or MAs, post-MA requirements 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, promotion and reimbursement vary from country to country. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. 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.

Non-Clinical Studies and Clinical Trials

Similar to the United States, the various phases of non-clinical and clinical research abroad are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of GLP, as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products, e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both *in vitro* and *in vivo*, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Council for Harmonization of Technical Requirements for Human Use, 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 advanced therapy medicinal products, or ATMPs. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity within the EU to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and

supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the EU Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. 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. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR transition period ended on January 31, 2025, and all clinical trials (and related applications) are now fully subject to the provisions of the CTR.

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 an MA. To obtain regulatory approval of an investigational chemical or biological product in the EU, we must submit an MAA. The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs – "Centralized MAs" and "National MAs."

"Centralized MAs" are issued by the European Commission through the centralized procedure, based on the opinion of the CHMP of the EMA, and are valid across the entire territory of the EU. The centralized procedure is compulsory for certain types of product candidates, such as: (i) medicinal products derived from biotechnology processes, such as genetic engineering, (ii) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative or autoimmune diseases, and other immune dysfunctions and viral diseases, (iii) designated orphan medicines and (iv) ATMPs, such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure is optional for product candidates containing a new active substance not yet authorized in the EU, or for product candidates that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

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.

"National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

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 Priority Medicine, or 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. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Moreover, in the EU, the European Commission may grant a so-called "conditional MA" prior to obtaining the comprehensive clinical data required 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.

An 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 an MA of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" MA. Thus, an 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. An 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. Upon receiving MA, reference products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial MA of the reference product in the EU. The overall ten-year market exclusivity period may be extended to a maximum of eleven years if during the first eight years of those ten years, the MA holder obtains an authorization for one or more

new therapeutic indications, which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit over existing therapies. However, there is no guarantee that a product will be considered by the EU regulatory authorities to be a new chemical or biological 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

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 its sponsor can establish that (1) the product 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 the necessary 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 designation entitles a party to incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized MA procedure. The application for orphan designation must be submitted before the MAA. The applicant will receive a fee reduction for the MAA if the orphan designation has been granted, but not if the designation is still pending at the time the MA is submitted. Upon grant of an MA and assuming the requirement for orphan designation are also met at the time the MA is granted, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that regulatory authorities cannot accept another MA or grant an MA or accept an application to extend an existing MA in respect of a similar medicinal product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan, or PIP. Orphan 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 which it received orphan designation, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the orphan designation threshold. Additionally, an MA may be granted to a similar product for the same indication at any time if (1) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior, (2) the applicant consents to a second orphan medicinal product application; or (3) 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 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 product candidate 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 MA 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 an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. 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 an 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.

Healthcare Reform

Political, economic and regulatory developments are occurring in the EU and may affect the ability of pharmaceutical companies to profitably commercialize their products, once approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or regulate post-approval activities and affect the ability of pharmaceutical companies to commercialize their products. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In the EU, potential reductions in prices and changes in reimbursement levels could be the result of different factors, including reference pricing systems, parallel distribution and parallel trade. It could also result from the application of external reference pricing mechanisms, which consist of arbitrage between low-priced and high-priced countries. Reductions in the pricing of medicinal products in one EU member state could affect the price in other EU member states.

Health Technology Assessment, or HTA, of medicinal products in the EU is an essential element of the pricing and reimbursement decision-making process in a number of EU member states. The outcome of HTA has a direct impact on the pricing and reimbursement status granted to the medicinal product. A negative HTA by a leading and recognized HTA body concerning a medicinal product could undermine the prospects to obtain reimbursement for such product not only in the EU member state in which the negative assessment was issued, but also in other EU member states.

In 2011, Directive 2011/24/EU was adopted at the EU level. This Directive establishes a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states. The network facilitates and supports the exchange of scientific information concerning HTAs. Further to this, on December 13, 2021, Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted. The Regulation entered into force in January 2022 and has been applicable since January 2025, with phased implementation based on the type of product (i.e., oncology and advanced therapy medicinal products as of 2025, orphan medicinal products as of 2028, and all other medicinal products by 2030). The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early,

and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

Brexit and the Regulatory Framework in the United Kingdom

The UK formally left the EU on January 31, 2020, commonly referred to as "Brexit". Since the end of the Brexit transition period on January 1, 2021, and the implementation of the Windsor Framework on January 1, 2025, the UK has not generally been directly subject to EU laws with respect to medicinal products. The EU laws that have been transposed into UK law through secondary legislation remain applicable in Great Britain (England, Scotland and Wales), however, new legislation such as the CTR is not applicable in Great Britain.

Since January 1, 2021, the MHRA has been the UK's standalone medicines and medical devices regulator. As a result of the Protocol on Ireland and Northern Ireland, different rules applied in Northern Ireland than in Great Britain; broadly, Northern Ireland continued to follow the EU regulatory regime. However, on January 1, 2025 a new arrangement called the "Windsor Framework" came into effect and reintegrated Northern Ireland under the regulatory authority of the MHRA with respect to medicinal products. The Windsor Framework removes EU licensing processes, and EU labeling and serialization requirements in relation to Northern Ireland, and introduces a UK-wide licensing process for medicinal products.

UK Clinical Trials

It is currently unclear to what extent the UK will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from pre-existing EU legislation (as implemented into UK law, through secondary legislation), and after Brexit, EU laws on clinical trials (including the CTR) are not directly applicable in Great Britain (i.e., the UK excluding Northern Ireland). The extent to which the regulation of clinical trials in the UK will mirror the CTR in the long term is not yet certain, however, on December 12, 2024, the UK government introduced a legislative proposal - the Medicines for Human Use (Clinical Trials) Amendment Regulations 2024 - that, if implemented, will replace the current regulatory framework for clinical trials in the UK. The legislative proposal aims to provide a more flexible regime to make it easier to conduct clinical trials in the UK, increase the transparency of clinical trials conducted in the UK and make clinical trials more patient centered. The UK government has provided the legislative proposal to the UK Parliament for its review and approval. Once the legislative proposal is approved (with or without amendment), it will be adopted into UK law which is expected in early 2026. Under the terms of the Protocol on Ireland and Northern Ireland, provisions of the CTR which relate to the manufacture and import of investigational medicinal products and auxiliary medicinal products currently apply in Northern Ireland.

UK Marketing Authorizations

MAs in the UK are governed by the UK's Human Medicines Regulations 2012 (as amended). All existing centralized procedure MAs were automatically converted into UK MAs effective in Great Britain (only), free of charge on January 1, 2021 (unless MA holders opted out of this scheme). Under the terms of the Windsor Framework, these MAs became valid for the whole of the UK from January 1, 2025. In order to use the centralized procedure to obtain an MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore, since Brexit, companies established in the UK can no longer 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 to obtain an MA to market products in the UK. Applications are governed by the UK's Human Medicines Regulations 2012 (as amended) and are made electronically through the MHRA Submissions Portal. In addition, an international recognition procedure, or IRP, has applied since January 1, 2024, whereby the MHRA will have regard to decisions on the approval of MAs made by the EMA and certain other regulators when determining an application for a new UK MA. Pursuant to the IRP, the MHRA will take into account the expertise and decision-making of trusted regulatory partners (i.e., the regulators in Australia, Canada, Switzerland, Singapore, Japan, the U.S. and the EU). The MHRA will conduct a

targeted assessment of IRP applications but retain the authority to reject applications if the evidence provided is considered insufficiently robust. The IRP allows medicinal products approved by such trusted regulatory partners that meet certain criteria to undergo a fast-tracked MHRA review to obtain and/or update an MA in the UK. Applications should be decided within a maximum of 60 days if there are no major objections identified that cannot be resolved within such 60-day period and the approval from the trusted regulatory partner selected has been granted within the previous 2 years or if there are such major objections identified or such approval has not been granted within the previous 2 years within 110 days. Applicants can submit initial MAAs to the IRP but the procedure can also be used throughout the lifecycle of a product for post-authorization procedures including line extensions, variations and renewals. In the UK, the initial duration of an MA is five years and following renewal will be valid for an unlimited period unless the MHRA decides on justified grounds relating to pharmacovigilance, to proceed with only one additional 5-year renewal. Any authorization which is not followed by the actual placing of the medicinal product on the market in the UK within 3 years shall cease to be in force.

Post Brexit, the MHRA has updated 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 and a rolling review process for MAAs (rather than a consolidated full dossier submission).

The UK's Human Medicines Regulations 2012 (as amended) allow the MHRA to grant an MA under exceptional circumstances in the UK. Such MA is intended for products for which the applicant can show that it is unable to provide comprehensive data on the efficacy and safety of the medicinal product under normal conditions of use because the condition to be treated is rare or because collection of full information is not possible or is unethical. This type of MA is similar to the MA under exceptional circumstances granted by the European Commission. Since the end of the Brexit transition period on January 1, 2021, applications for MAs under exceptional circumstances in Northern Ireland were required to be submitted to the EMA. However, since the implementation of the Windsor Framework on January 1, 2025, such applications are now required to be submitted to the MHRA that will grant UK-wide MAs under exceptional circumstances. The MHRA may take into account an MA under exceptional circumstances granted by the European Commission or by a competent authority in another jurisdiction when determining an application for an MA under exceptional circumstances, but the final decision on the approval of such application will rest with the MHRA. The MHRA is likely to impose specific obligations on the holder of an MA under exceptional circumstances (i.e., to provide information on the safe and effective use of the product). The MHRA will communicate these obligations to the applicant during its review of the application. This authorization route does not normally lead to a standard MA.

UK Orphan Designation

Post-Brexit, the UK has retained the EU Regulation which governs the designation of medicinal products as orphan medicinal products and which establishes incentives thereto (Regulation (EC) No. 141/2000) as part of UK law by virtue of the EU (Withdrawal) Act 2018.

There is no pre-MA orphan designation in the UK. The MHRA reviews applications from companies for orphan designation in parallel to the corresponding MAA. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in the UK, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period of market exclusivity will be set from the date of first approval of the product in the UK.

UK Specials Regulation

The UK's Human Medicines Regulations 2012 (as amended) 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 countries in which we may sell, market and distribute products for which we obtain marketing approval. These laws and regulations cover data privacy and the protection of health-related and other personal data. Laws and regulations in the EU and other jurisdictions apply broadly to the collection, use, storage, disclosure, processing and security of personal data, and have generally become more stringent over time.

For example, the EU General Data Protection Regulation, or GDPR, imposes strict requirements for processing the personal data of individuals within the EEA or in the context of our activities in the EEA. 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 million or up to 4% of the total worldwide annual turnover of a noncompliant undertaking in the preceding financial year, whichever is higher, and other administrative penalties and may expose us to compensation claims from affected individuals.

Further, from January 1, 2021, we are subject to the GDPR and also the UK General Data Protection Regulation, which, together with the amended UK Data Protection Act 2018 (collectively, the UK GDPR), retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, e.g. fines up to the greater of £17.5 million or 4% of the total worldwide annual turnover of a noncompliant undertaking for the preceding financial year. The European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EU member states to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews/extends that decision, and it continues to remain under review by the Commission during this period.

Employees

As of December 31, 2024, we had 381 employees, 375 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 ordinary shares 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 ordinary shares could decline. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

Risks Related to Our Financial Position and Need for Additional Capital

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

We are a clinical stage company with limited operating history. We were formed and began operations in 2015. We have never been profitable and do not expect to be profitable in the foreseeable future. We have incurred net losses since inception, including net losses of approximately $147.8 million and $84.0 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of approximately $702.0 million. Since our inception, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facilities and plasmid and DNA production facility, developing manufacturing processes, advancing the product candidates in our ophthalmology, salivary gland and neurodegenerative disease programs, research and development activities, including our riboswitch gene regulation platform technology, building our intellectual property portfolio, organizing and staffing our company, developing our business plans, raising capital, securing debt financing 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, if ever, 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 ongoing Phase 2 AQUAx2 clinical trial of AAV-hAQP1 for the treatment of patients with radiation-induced xerostomia. In addition, we expect to continue incurring increasing research and development costs associated with our clinical activities for AAV-GAD for the treatment of Parkinson's disease and research, preclinical and clinical activities for our riboswitch platform. 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 whether we will be able to begin generating revenue from the commercialization of products or achieve or maintain profitability.

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 FDA, MHRA, 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.

There is no guarantee that we will receive in a timely fashion or at all the additional milestone payments contemplated under the Asset Purchase Agreement or the revenues associated with our manufacture of the commercial supply of the RPGR Product under the Supply Agreement.

On December 20, 2023, we and MeiraGTx UK II Limited entered into and consummated the Asset Purchase Agreement with Johnson & Johnson Innovative Medicine pursuant to which we sold and assigned to Johnson & Johnson Innovative Medicine, and Johnson & Johnson Innovative Medicine purchased and assumed, the UCLB RPGR License Agreement relating to the research, development, manufacture and exploitation of the RPGR Product, and other related assets as described in the Asset Purchase Agreement. MeiraGTx UK II Limited and Johnson & Johnson Innovative Medicine also entered into a Supply Agreement on December 20, 2023 pursuant to which MeiraGTx UK II Limited, together with its affiliates, will manufacture commercial supply of the RPGR Product for Johnson & Johnson Innovative Medicine for an initial term of four years, with Johnson & Johnson Innovative Medicine having an option to extend the Supply Agreement for a fifth year upon written notification to us.

Under the Asset Purchase Agreement, Johnson & Johnson Innovative Medicine paid us a non-refundable upfront cash purchase price of $65.0 million in December 2023. Additionally, pursuant to and subject to the terms and conditions set forth in the Asset Purchase Agreement, Johnson & Johnson Innovative Medicine agreed to pay us future contingent consideration of up to an aggregate of $350.0 million, as follows: (i) a milestone payment of $50.0 million in connection with the achievement of the initiation of the extension study for the Phase 3 LUMEOS clinical trial for the RPGR Product; (ii) $10.0 million upon completion of certain specified development services for the drug substance for the RPGR Product; (iii) $5.0 million upon completion of certain specified development services for the drug product for the RPGR Product; (iv) $175.0 million upon the first commercial sale of an RPGR Product in the United States; (v) $75.0 million upon the first commercial sale of an RPGR Product in at least one of the United Kingdom, France,

Germany, Spain and Italy; (vi) $25.0 million upon completion of the transfer of certain manufacturing technology for drug substance and drug product from us to Johnson & Johnson Innovative Medicine; and (vii) $10.0 million upon regulatory approval of a Johnson & Johnson Innovative Medicine-selected manufacturing facility in each of the United States and European Union for commercial manufacture of the RPGR Product. As of December 31, 2024, we have received $60.0 million in milestone payments from Johnson & Johnson Innovative Medicine.

In connection with the sale and assignment of the UCLB RPGR License Agreement relating to the research, development, manufacture and exploitation of the RPGR Product to Johnson & Johnson Innovative Medicine, Johnson & Johnson Innovative Medicine has control and broad discretion over all aspects of the development and commercialization of the RPGR Product and we will have little, if any, influence over how such activities will be conducted. Johnson & Johnson Innovative Medicine will also be responsible for seeking regulatory approval and initiating the first commercial sale in the relevant jurisdictions of the RPGR Product, as well as obtaining regulatory approval of its manufacturing facilities in the relevant jurisdictions for the purposes of conducting commercial manufacture of the RPGR Product. These regulatory approvals and initiation of the first commercial sales in the relevant jurisdictions would entitle us to receive milestone payments up to an aggregate of $260.0 million. Our receipt of these milestones is dependent on Johnson & Johnson Innovative Medicine's ability to successfully develop and commercialize the RPGR Product and obtain the necessary regulatory approvals for its manufacturing facilities. If these regulatory approvals or commercial sales do not occur in a timely fashion or at all, then such milestone payments, and any revenues we may receive from manufacturing commercial supply of the RPGR Product, may be delayed or we may not receive such payments. Additionally, certain of these milestone based payments are payable upon our achievement of the specified development services, completion of the transfer of certain manufacturing technology to Johnson & Johnson Innovative Medicine and our ability to manufacture sufficient commercial supply of the RPGR Product in a timely fashion. In the event we are not successful in completing these activities in a timely fashion or at all, we will not receive the milestone payments associated with the relevant milestone under the Asset Purchase Agreement or receive revenue for commercial supply of the RPGR Product under the Supply Agreement. In each of these circumstances, our anticipated cash inflows from these activities would be reduced or eliminated, which would have an adverse effect on our revenue and financial position.

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 has been and may in the future be adversely affected by external factors beyond our control, including changes in the political climate, geopolitical actions, changes in market interest rates, potential reforms and changes to government regulations, 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 and strategic alliances and licensing arrangements. 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 has diverted and may in the future 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, 2024, our cash, cash equivalents and restricted cash were $105.7 million. In addition, we expect to receive $0.7 million from receivables from Johnson & Johnson Innovative Medicine during the first quarter of 2025 in connection with transition services we provided to Johnson & Johnson Innovative Medicine. Based on our cash, cash equivalents, accounts receivable – related

party and tax incentive receivable at December 31, 2024, together with the proceeds from the anticipated closing of the strategic collaboration with Hologen Ltd, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into 2027 and to repay our debt obligation of $75.0 million to Perceptive (due in August 2026). This estimate does not include the $285.0 million in milestones we are eligible to receive under the Asset Purchase Agreement upon first commercial sale of an RPGR Product in the United States and in at least one of the United Kingdom, France, Germany, Spain and Italy, for completion of the transfer of certain manufacturing technology to Johnson & Johnson Innovative Medicine and upon regulatory approval of a Johnson & Johnson Innovative Medicine-selected manufacturing facility in each of the United States and European Union for commercial manufacture of the RPGR Product. 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, such as inflation or other factors that may significantly increase our business costs. 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 clinical development for our radiation-induced xerostomia product candidate, AAV-hAQP1, and for our product candidate for the treatment of Parkinson's disease, AAV-GAD;

- the progress, timing, costs and results of our ongoing clinical development for our AAV-AIPL1 gene therapy product candidate, our CNGB3 achromatopsia gene therapy product candidate, AAV-CNGB3, for our CNGA3 achromatopsia gene therapy product candidate, AAV-CNGA3, and for our RPE65-associated retinal dystrophy product candidate, AAV-RPE65;

- 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-hAQP1, and our product candidate for the treatment of neovascular age related macular degeneration, or wet AMD;

- the development of our potentially transformative riboswitch gene regulation platform technology designed to precisely and specifically control gene therapy expression levels via dose-response to orally delivered small molecules;

- the extent to which we receive the milestone payments under the Asset Purchase Agreement with Johnson & Johnson Innovative Medicine;

- continuing our current research programs and our preclinical development of product candidates from our current research programs;

- 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;

- 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 facilities 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 shareholder. For example, in connection with entering into the Financing Agreement (as defined below), we issued warrants to Perceptive (as defined below), to purchase 400,000 ordinary shares at an exercise price of $15.00 per share and 300,000 ordinary shares at an exercise price of $20.00 per share. Additional debt financing or preferred equity financing, if available, may involve agreements that include covenants further 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 may not have sufficient cash flows or cash on hand to satisfy our debt obligations or covenants under our financing arrangements, or we may not be able to effectively manage our business in compliance with such covenants.

On August 2, 2022, we, as borrower, and our wholly-owned subsidiaries MeiraGTx UK II Limited and MeiraGTx Ireland DAC, as guarantors (the "Subsidiary Guarantors"), entered into a senior secured financing arrangement (the "Financing Agreement") by and among us, the Subsidiary Guarantors, the lenders and other parties from time to time party thereto and Perceptive Credit Holdings III, LP, as administrative agent and lender ("Perceptive"). On December 19, 2022, the Financing Agreement was converted to a notes purchase agreement and guaranty (as converted, the "Notes Purchase Agreement") between the same parties and under substantially the same terms and conditions as the Financing Agreement, subject to certain customary note constitution terms. We and the Subsidiary Guarantors entered into a Consent and Amendment with Perceptive on August 10, 2023 (the "First Consent

and Amendment), and we and the Subsidiary Guarantors entered into a second Consent and Amendment with Perceptive on December 20, 2023 (the "Second Consent and Amendment"). The Notes Purchase Agreement provides for an initial $75.0 million notes issuance (the "Tranche 1 Notes"). Pursuant to the First Consent and Amendment, we were able to request in our sole discretion, and Perceptive agreed to subscribe to purchase upon such request, an additional $25.0 million notes issuance (the "Tranche 2 Notes", together with the Tranche 1 Notes, the "Notes") at any time before August 2, 2024, subject to the terms of the Notes Purchase Agreement. Previously, the Company's request for issuance of the Tranche 2 Notes was to be determined at Perceptive's sole discretion. Under each of the First Consent and Amendment and the Second Consent and Amendment, the Notes Purchase Agreement was also amended to increase the applicable early redemption fee. The Notes incur interest, subject to certain provisions therein, at a fluctuating rate per annum equal to 10.00% plus the secured overnight financing rate administered by the Federal Reserve Bank of New York for a one-month tenor, subject to a 1.00% floor. The Notes Purchase Agreement matures on August 2, 2026 and is interest-only during the term. The Notes Purchase Agreement also contains various restrictions and covenants, including, among other things, covenants regarding the incurrence of additional indebtedness, limitations on liens, limitations on certain investments, limitations on making distributions, dividends and other payments, mergers, consolidations and acquisitions, dispositions of assets, maintenance of at least $3.0 million in a U.S. bank account, transactions with affiliates, changes to governing documents, changes to certain agreements and leases and changes in control. Our obligations under the Notes Purchase Agreement are secured by our London, UK and Shannon, Ireland manufacturing facilities, $3.0 million of our cash and the bank accounts of the Subsidiary Guarantors, and the issued and outstanding equity interests of the Subsidiary Guarantors.

There can be no assurance that our cash and cash equivalents available under the Notes Purchase Agreement and under any future financings, together with any funds generated by our operations, will be sufficient to satisfy our debt payment obligations. Our inability to generate funds, obtain financing sufficient to satisfy our debt payment obligations or remain in compliance with the debt covenants may result in such obligations being accelerated by our lenders, which would likely have a material adverse effect on our business, financial condition and results of operations.

The covenants may restrict our current and future operations, particularly our ability to respond to certain changes in our business or industry, or take future actions. Additionally, our ability to comply with these restrictive covenants may be impacted by events beyond our control, such as economic conditions or major central bank policy actions. Our Notes Purchase Agreement provides that our breach or failure to satisfy certain covenants constitutes an event of default. Upon the occurrence of an event of default, in addition to an increase in the rate of interest on the Notes of 3% per annum, Perceptive could elect to declare all amounts outstanding thereunder to be immediately due and payable, proceed against the assets we provided as collateral, and, if such debt were accelerated, we may not have sufficient cash on hand or be able to sell sufficient collateral to repay it, which would have an immediate adverse effect on our business and operating results. This could potentially cause us to cease operations and result in a complete loss of your investment in our ordinary shares.

Our review of potential strategic transactions may not result in an executed or consummated transaction or other strategic alternative and may not result in anticipated benefits to us or our shareholders, and the process of reviewing strategic transactions or its conclusion could be disruptive and distracting to our business operations and management.

We have, and may continue to, opportunistically identify and evaluate strategic opportunities regarding our assets. For example, in October 2023, we entered into the Investment Agreement with Sanofi Foreign Participations, pursuant to which, among other things and subject to the terms and conditions specified therein, we issued an aggregate of 4,000,000 ordinary shares, at a purchase price of $7.50 per share for gross proceeds of $30.0 million. Sanofi also received a right of first negotiation (ROFN) for the use of our riboswitch gene regulation technology for certain Central Nervous System (CNS) and Immunology and Inflammation (I&I) targets, including IL-4 and IL-13, as well as for GLP-1 and other gut peptides for obesity, and for our Phase 2 xerostomia program. In addition, in December 2023, we announced the transaction with Johnson & Johnson Innovative Medicine, as described above. There can be no assurance that we will be successful in our efforts to pursue or advance such options, or identify similar opportunities, or that any potential transaction would be consummated or, if consummated, will provide the anticipated benefits to us or otherwise enhance shareholder value. Any such potential transaction would be dependent upon a number of factors beyond our control, including, without limitation, market conditions, industry trends, the interest of third parties in our assets and whether the terms of any strategic transaction would be acceptable to us. The process of reviewing potential strategic alternatives is time consuming and may be distracting and disruptive to our business operations and long-term planning, which may cause concern to our current or potential customers, employees, investors, strategic partners and other constituencies and may have a material impact on our business and operating results or result in increased volatility in our share price.

We are heavily dependent on the success of our 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, manufacture, 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-hAQP1, AAV-GAD, AAV-AIPL1 and our riboswitch gene regulation technology platform, as well as potentially AAV-CNGB3, AAV-CNGA3, AAV-RPE65, 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. We cannot be certain that our 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 product candidates from the FDA, MHRA or other regulatory bodies, we cannot be certain that our product candidates will be successfully commercialized by us or any of 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 and other regulatory authorities. We are not permitted to market our product candidates in the United States until they receive approval of a BLA from the FDA, we cannot market them in the UK or EU until we receive approval for an MA, from the MHRA or European Commission, respectively, and we cannot market them in other countries until we receive any other required regulatory approval in those countries.

Because some of our product candidates are based on similar technology, 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

It is difficult to predict the time and cost of product candidate development on our novel gene therapy platform. A limited number of 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, a limited number of 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, a limited number of therapeutic products have received approval from the FDA or an MA from the MHRA and European Commission. 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 Therapeutic Products 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 may also be subject to review and oversight by an institutional biosafety committee 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 the EU, 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 MA 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 MA 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 the UK 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. Definitions for individual classes of ATMPs remain unchanged and classification of ATMPs are undertaken by the MHRA. 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 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 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 or conditions in which there may be limited clinical experience with novel endpoints and methodologies, there is heightened risk that the FDA, MHRA, EMA or other regulatory bodies may not consider the clinical trial endpoints we pursue 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 an MAA, 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 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, be able to 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 consensus with the FDA, MHRA or other regulatory authorities as to the design or implementation of our clinical trials and obtaining regulatory allowance or approval to commence a clinical trial;
- inability to reach 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;
- our inability to recruit and train clinical trial investigators with the appropriate competencies and experience to conduct the clinical trials, administer our product candidates and oversee clinical trial staff;
- delays in obtaining IRB or ethics committee approval or positive opinion at each site;
- inability to recruit suitable patients to participate in a clinical trial;
- inability to develop and validate any companion diagnostic we may decide to use in connection with a clinical trial, if applicable;
- delays in sufficiently developing, designing and manufacturing equipment or medical devices used to administer our product candidates in our clinical trials, if applicable;
- patients not completing a clinical trial or returning for post-treatment follow-up;
- clinical sites, CROs, or other third parties deviating from trial protocol or dropping out of a trial;

- failures to conduct clinical trials in accordance with good clinical practice, or GCP, requirements, or other applicable regulatory guidelines;

- addressing patient safety concerns that arise during the course of a trial, including occurrence of adverse events associated with the product candidate;

- having an insufficient number of clinical trial sites; or

- inability to manufacture sufficient quantities of our product candidates for use in clinical trials, or to manufacture such product candidates to acceptable quality standards.

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, 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 or other foreign 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 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 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. For example changes in the leadership of the FDA and other federal agencies under the current presidential administration or reductions in funding, operations, staffing and policies of the FDA and other federal agencies could impact our clinical development plans and timelines.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the

EU has evolved over recent years. As of January 2025, clinical trials (and related applications) in the EU are now fully subject to the provisions of the CTR, which allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state and provides for a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our development plans.

It is currently unclear to what extent the UK will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from pre-existing EU legislation (as implemented into UK law, through secondary legislation). The extent to which the regulation of clinical trials in the UK may mirror the (EU) CTR in the long term is not yet certain. In December 2024, the UK government introduced a legislative proposal which, if implemented, could provide a more flexible regime to make it easier to conduct clinical trials in the UK, increase the transparency of clinical trials conducted in the UK and make clinical trials more patient centered. The legislation may not be approved or could be approved with amendment, and any adoption into UK law may not be until early 2026. Under the terms of the Protocol on Ireland and Northern Ireland, provisions of the (EU) CTR which relate to the manufacture and import of investigational medicinal products and auxiliary medicinal products currently apply in Northern Ireland. A decision by the UK not to closely align its regulations with the new approach adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be impacted.

Pandemics, epidemics or outbreaks of an infectious disease have impacted and may in the future materially and adversely impact our business, including our preclinical studies, clinical trials, manufacturing capabilities and regulatory approvals.

We have and may in the future experience disruptions from pandemics, epidemics or outbreaks of an infectious disease that could severely impact our business, preclinical studies, clinical trials and laboratory and manufacturing activities, including, for example, 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, interruption of key clinical trial activities due to limitations on travel imposed or recommended by regulatory authorities or others, interruption or delays in the operations of the FDA, MHRA, EMA or other regulatory authorities, interruption of, or delays in, the manufacturing of our product candidates, 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, and interruption or delays to our sourced discovery and clinical activities. For example, as a result of the COVID-19 pandemic, we restricted onsite activities and also experienced some delays in enrolling, treating and monitoring patients in our clinical trials, as well as limited disruptions to our supply chain.

The extent to which any future outbreaks or any variants of COVID-19 or another pandemic may 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 any pandemic, the timing, distribution and effectiveness of vaccines, vaccination rates, travel restrictions and physical distancing requirements 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 any such 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. Furthermore, the magnitude of the economic impact of any pandemic including sustained inflation, supply chain

disruptions, and major central bank policy actions may result in significant disruption of global financial markets, which could materially affect our performance, financial condition, results of operations, and cash flows, as well as our ability to raise additional capital. Additionally, major central bank policy actions may have a negative impact on our payment obligations under the Notes Purchase Agreement.

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. 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, on November 28, 2023, the FDA announced that it was investigating reports of T-cell malignancies, including CAR- positive lymphoma, in patients who received treatment with BCMA- or CD19-directed autologous CAR-T cell immunotherapies, and in January 2024, the FDA required the manufacturers of certain CAR-T therapies to add boxed warnings to product labeling cautioning against the risk of T-cell malignancies. Although none of our current product candidates utilize the same technology as these CAR-T immunotherapies, 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.

We may fail to maintain the benefits of certain regulatory designations that we have obtained for our product candidates, and may in the future seek and fail to obtain such designations for other of our current or potential future product candidates. Even if such designations are obtained, they may not lead to faster development or regulatory review or approval, and they do 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 drugs and biological products that meet certain criteria. For example, the FDA has a Fast Track designation program that is intended to expedite or facilitate the process for reviewing product candidates that meet certain criteria. Specifically, investigational drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical needs. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the review team during product development and, once a BLA is submitted, the application may be eligible for priority review. In addition, the Fast Track product may be eligible for rolling review, where the FDA may consider for review sections of the BLA 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. Even if Fast Track designation is granted, it may be rescinded if the product no longer meets the qualifying criteria. In August 2018, AAV-CNGB3 was issued Fast Track designation by the FDA for the treatment of achromatopsia caused by CNGB3 mutations. In January 2021, AAV-CNGA3 was issued Fast Track designation 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.

A sponsor may also seek an RMAT designation 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 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 the FDA to discuss the development plan for the product candidate, and eligibility for rolling review and priority review, provided the applicable criteria are met. 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. In December 2024, the FDA granted RMAT designation to AAV-hAQP1 for the treatment of grade 2 or 3 radiation-induced xerostomia.

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 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, as applicable.

We have received orphan drug designation and orphan designation from the FDA and European Commission, respectively, for AAV-CNGB3, AAV-CNGA3, AAV-RPE65, AAV-AIPL1, AAV-RDH12 and orphan drug designation from the FDA for AAV-hAQP1 and AAV-BBS10, and we may seek orphan drug designation or orphan designation for additional product candidates in the future, but any orphan drug designations or orphan 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 candidate 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 European Commission grants orphan designation on the basis of the EMA's Committee for Orphan Medicinal Products opinion. 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.

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 disease or condition for which it has orphan drug 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 disease or condition 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 designation entitles a party to financial incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized MA procedure. Moreover, upon grant of an MA and assuming the requirement for orphan designation are also met at the time the MA is granted, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. This period may be reduced to six years if, at the end of the fifth year, the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market

exclusivity, or where the prevalence of the condition has increased above the orphan designation threshold. In the EU, an MA for an orphan designated product will not be granted if a similar product has been approved in the EU for the same therapeutic indication, unless the applicant can establish that (i) its product, although similar to the orphan medicinal product already authorized is safer, more effective or otherwise clinically superior; (ii) the MA holder for the orphan medicinal product grants its consent; or (iii) if the MA holder of the orphan medicinal product is unable to supply sufficient quantities of product. A similar medicine 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.

There is no pre-MA orphan designation in the UK. The MHRA reviews applications from companies for orphan designation in parallel to the corresponding MAA. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in the UK, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in the UK.

We have obtained orphan drug designation from the FDA and orphan designation from the European Commission 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-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-hAQP1 for the treatment of grade 2 and grade 3 late xerostomia from parotid gland hypofunction caused by radiotherapy and for AAV-BBS10 for the treatment of Bardet-Biedel syndrome (BBS) due to *BBS10* mutations. We may seek orphan drug designation and orphan designation for other current and future product candidates. Even with orphan drug designation and orphan 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 and the EU may be unavailable if we seek approval for a disease or condition broader than the orphan drug-designated and orphan-designated disease or condition or may be lost in the United States or EU if the FDA or foreign authorities later determine 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 biologics with different active principal molecular structural features can be approved for the same disease or 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 disease or condition if the FDA concludes that the later product is safer, more effective, makes a major contribution to patient care, or if the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Likewise, in the EU and UK, the European Commission or MHRA, respectively, can authorize a similar product for the same therapeutic indication, if it concludes that the later product is safer, more effective or clinically superior; if the MA holder for the initial orphan medicinal product grants its consent; or if such MA holder is unable to supply sufficient quantities of the product. Neither orphan drug designation nor orphan designation 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 and orphan designation for other existing and future product candidates, we may never receive such designations.

The FDA has granted rare pediatric disease designation to a number of our gene therapy product candidates, however, there is no guarantee that FDA approval of any of these gene therapy candidates will result in a priority review voucher.

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease drugs and biologics intended to treat certain orphan diseases affecting fewer than 200,000 patients in the U.S., the serious or life-threatening manifestations of which primarily affect individuals aged 18 years of age or younger, or affects more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for such disease or condition will be recovered from sales in the U.S. of such drug. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" that meets certain criteria may be eligible to receive a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor, and such priority review vouchers have recently sold for between $100 million to $158 million. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

The FDA has granted us rare pediatric disease designation for AAV-AIPL1 for the treatment of Leber congenital amaurosis (LCA4) retinal dystrophy, AAV-BBS10 for the treatment of BBS due to *BBS10* mutations, AAV-RDH12 for the treatment of Leber congenital amaurosis (LCA) and early-onset severe retinal dystrophy (EOSRD), AAV8-RK-RetGC for the treatment of patients with Leber congenital amaurosis due to *GUCY2D* mutations (LCA1), AAV-RPE65 for the treatment of inherited retinal dystrophy due to biallelic *RPE65* mutations, AAV-CNGB3 for the treatment of achromatopsia caused by mutations in the *CNGB3* gene and AAV-CNGA3 for the treatment of achromatopsia caused by mutations in the *CNGA3* gene. There is no guarantee that we will be able to obtain a priority review voucher, even if one or more of these gene therapy product candidates is approved by the FDA. Under the current statutory provisions, the FDA may not award a rare pediatric disease priority review voucher to sponsors of marketing applications unless the drug has received rare pediatric disease designation as of December 20, 2024 and is approved by the FDA no later than September 30, 2026. Even though we received rare pediatric disease designation by the current statutory deadline of December 20, 2024 for all of these gene therapy product candidates except AAV8-RK-RetGC, which received such designation in January 2025, we may not receive a voucher for such gene therapy product candidates if we do not obtain approval by September 2026. It is possible that Congress may retroactively extend the date by which a rare pediatric disease-designated drug may be designated as such to be eligible for a priority review voucher, or extend the date by which a rare pediatric disease-designated drug must obtain approval in order to receive a priority review voucher, but even if such legislation is enacted, we may not obtain approval by that date, and even if we do, we may not obtain a priority review voucher.

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 also have GMP manufacturing facilities in London, United Kingdom and Shannon, Ireland, which we expect can supply our current clinical and preclinical programs, as well as our third party supply obligations, through regulatory approval and, should they be approved, provide sufficient capacity for their commercial production. However, if we experience slowdowns or problems with our facilities or 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 GMP. 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. Generally, our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must successfully complete a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or the product candidates that we manufacture for third parties. In addition, certain regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or the product candidates that we manufacture for third parties or the associated quality systems for compliance with the regulations applicable, if and when approved, to the activities being conducted. If these facilities do not successfully complete a pre-approval plant inspection, FDA, MHRA or other regulatory approval of the product candidates 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 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. Regulatory agencies may also require additional studies if a new manufacturer is relied upon for clinical or 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, failure of manufacturing equipment or systems 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 facilities in London, United Kingdom and Shannon, Ireland, we may lease, operate, purchase, or construct additional facilities to supply our clinical and preclinical programs, as well as to meet our third party supply obligations, or conduct expanded manufacturing or other related activities in the future. Expanding our manufacturing capacity to produce the preclinical, clinical and commercial supply of our products and their components, as well as our obligations under the Supply Agreement with Johnson & Johnson Innovative Medicine if the RPGR Product is successfully commercialized, has required and will continue to require substantial additional expenditures, time, and various regulatory approvals and permits, as well as hiring, training and retraining employees and managerial personnel to staff our manufacturing and supply chain operations. Start-up costs can be large and may exceed our expectations, 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, establish or sustain sufficient manufacturing capabilities or manufacture our products economically or in compliance with GMP 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. 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, 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. Furthermore, although we have conducted and may in the future conduct natural history studies to better characterize the patient populations we seek to address, any natural history studies we may undertake could 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.

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, MHRA 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, the DSMB, or other regulatory bodies could suspend or terminate our clinical trials or the FDA, MHRA 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 or similar risk management measures;
- 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, competent authorities in the EU 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, European Commission 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. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not expected before early 2026. The revisions may however have a significant impact on the pharmaceutical industry in the long term.

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 of an MAA from the MHRA or European Commission, 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 other foreign regulatory agencies, that such product candidates are safe and effective for their intended uses, or with respect to biologics in the United States, that such product candidates are safe, pure, and potent 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, European Commission 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, or other foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

Even if we obtain FDA, MHRA or European Commission approval for our product candidates in the United States, UK or EU, we may never obtain approval for or commercialize them 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 competent authorities 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 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 GMP and similar 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 other regulatory authorities 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 other regulatory authorities impose 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 healthcare fraud and abuse laws, as well as state consumer protection laws. Similar risks apply in foreign jurisdictions.

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 manufacturing processes or third-party manufacturers, 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 and foreign regulatory authorities' 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 be subject to enforcement action, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Interim, "topline" 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 publicly disclose preliminary or topline data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the topline or preliminary

data we previously published. As a result, topline and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our clinical trials. Interim data from these trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as subject enrollment continues and more data become available. Adverse differences between interim data and topline, preliminary, or final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our ordinary shares.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

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 and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, disruptions caused by global health concerns, ability to hire and retain key personnel, including those with experience relating to novel gene therapy product candidates, acceptance of the payment of user fees, statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities 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 such as the EMA, following its relocation to Amsterdam and related reorganization (including staff changes), may also slow the time necessary for new product candidates to be reviewed and/or approved, which would adversely affect our business. For example, in recent years, 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. In addition, the current presidential administration has threatened to

lay off thousands of federal health workers, including at the FDA, which may delay review times for approval of our product candidates and impact our ability to correspond with the FDA regarding the development of our programs in a timely fashion.

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 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. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted, including aggregate reductions of Medicare payments to providers, which was temporarily suspended from May 1, 2020 through March 31, 2022, and reduced payments to several types of Medicare providers. In March 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminated the statutory Medicaid drug rebate cap for single source and innovator multiple source drugs, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

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. In August 2022, the IRA was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare beginning in 2026, with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new manufacturer discounting program (which began in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. CMS has published the negotiated prices for the initial ten drugs, which will first be effective in 2026, and the list of the subsequent 15 drugs that will be subject to negotiation, although the Medicare drug price negotiation program is currently subject to legal challenges. While the impact of the IRA on the pharmaceutical industry cannot yet be fully determined, it is likely to be significant. For that and other reasons, it is currently unclear how the IRA will be effectuated. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other healthcare 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. 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, drug price reporting and other transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Some states have enacted legislation creating so-called prescription drug affordability boards, which ultimately may attempt to impose price limits on certain drugs in these states. 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. 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 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 healthcare 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.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted in the EU. The Regulation entered into force in January 2022 and has been applicable since January 2025, with phased implementation based on the type of product (i.e., oncology and advanced therapy medicinal products as of 2025, orphan medicinal products as of 2028, and all other medicinal products by 2030). The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

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 laws 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, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for 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 non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives), 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 regulation and other legal obligations relating to data privacy and protection. Compliance with these requirements is complex and costly. The actual or perceived failure to comply with such obligations could materially harm our business.

The global data protection landscape is continually evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, access to, confidentiality, disclosure, storage, processing, retention and security of personal information such as information that we may collect in connection with clinical trials in the U.S. and abroad.

In the U.S., HIPAA imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon "covered entities" (health plans, healthcare clearinghouses and certain healthcare 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, as well as their covered subcontractors. Most healthcare providers, including research institutions and other vendors from which we may obtain health-related information, are subject to privacy and security regulations promulgated under HIPAA. We do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information.

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. Further, we may also be subject to other state laws governing the privacy, processing and protection of personal information. For example, the CCPA requires covered businesses that process the personal information of California residents to, among other things: provide certain disclosures to California residents regarding the business's collection, use, and disclosure of their personal information; receive and respond to requests from California residents to access, delete, and correct their personal information, or to opt out of certain disclosures of their personal information; and enter into specific contractual provisions with service providers that process California resident personal information on the business's behalf. Similar laws have been passed in other states, and are continuing to be proposed at the state and the federal level, reflecting a

trend toward more stringent privacy legislation in the United States. HIPAA, the CCPA and other domestic privacy and data protection laws and regulations may increase our compliance costs and potential liability.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For example, the GDPR imposes stringent requirements for processing the personal data of individuals within the EEA or in the context of our activities within the EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and, among other things, potential fines for noncompliance of up to €20 million or up to 4% of the total worldwide annual turnover of the relevant undertaking in the preceding financial year, whichever is higher, and other administrative penalties.

Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the U.S. Case law from the Court of Justice of the European Union states that reliance on the standard contractual clauses – a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism – alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case-by-case basis. The European Commission adopted its Adequacy Decision in relation to the new EU-US Data Privacy Framework ("DPF") on July 10, 2023, rendering the DPF effective as a GDPR transfer mechanism to U.S. entities self-certified under the DPF. We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue. In particular, we expect the adequacy of the DPF as an approved GDPR transfer mechanism to be challenged and international transfers to the United States and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. If, owing to the restriction or perceived restriction of personal data transfers, 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.

Further, we are subject to the UK GDPR, which imposes separate but similar obligations to those under the GDPR and comparable penalties, including fines of up to £17.5 million or 4% of a noncompliant undertaking's global annual revenue for the preceding financial year, whichever is greater. On October 12, 2023, the UK Extension to the DPF came into effect (as approved by the UK Government), as a data transfer mechanism from the UK to U.S. entities self-certified under the DPF. UK privacy law has been, and continues to be, subject to scrutiny and proposed changes. This could affect the ease of data transfers between the EEA and the UK in the future. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

Although we work to comply with applicable laws, regulations and standards, as well as our contractual obligations and other legal obligations, relating to data privacy and security, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction and/or organization to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy data and security concerns, even if unfounded, could result in additional costs, claims by and liability to third parties, government investigations and enforcement actions, damage to our reputation, and other adverse affects on our business, financial condition and results of operations.

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. Additionally, if environmental regulations are enacted that restrict our ability to use one or more of the materials or compounds necessary to manufacture our product candidates, and we are unable to find suitable alternatives or such alternatives require additional testing or will extend the manufacturing timeline, then we may be unable to manufacture our product candidates in a timely manner, or at all.

We may be subject to 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, our production efforts or those of our third-party manufacturers 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. Differences in the scientific approaches may create confusion or uncertainty among clinical trial investigators or patient populations, which could delay or hinder enrollment or initiation of our clinical trials.

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, 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., and Eli Lilly and Company. 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, manufacturing 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 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 healthcare, 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. 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-hAQP1, AAV-GAD, our IRD programs, our riboswitch gene regulation platform technology 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 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. 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 data privacy and security 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 emergencies, 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.

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. Jurisdictions outside the United States have established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the EU has had an established regulatory pathway for biosimilars since 2006. 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 GMP manufacturing facilities are unable to supply our product candidates for all of our current preclinical, clinical and potential commercial needs, including our third party supply obligations, we will be forced to seek out third-party manufacturers. We currently contract with third parties for the manufacture of plasmid used in producing 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 GMP viral vector manufacturing facility in London, UK, completed in early 2018, and our second, large scale GMP viral vector manufacturing facility and our first GMP plasmid and DNA production facility came online in 2022 in Shannon, Ireland. However, if our current facilities are damaged, suffer any form of delay or regulatory challenges, we experience slowdowns or problems with our facilities or we are unable to scale our internal manufacturing capabilities to meet demand for our product candidates, we will need to contract with third-party manufacturers to produce our product candidates. We have also agreed to manufacture commercial supply of the RPGR Product for Johnson & Johnson Innovative Medicine, if and when approved, under the Supply Agreement. If we fail to meet our obligations under the Supply Agreement, we may not be able to find a third-party manufacturer suitable to us or Johnson & Johnson Innovative Medicine to perform such manufacturing obligations, which could negatively impact our receipt of revenues under the Supply Agreement. While we now have our own plasmid manufacturing capabilities in our Shannon, Ireland facilities, we also rely on third-party manufacturers from time to time for the manufacture of plasmid used in the production of some 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 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.

We and our third-party manufacturers may not be able to comply with GMP regulations or similar regulatory requirements that might be required by the FDA, MHRA 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 GMP or similar 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 the Collaboration Agreement with Johnson & Johnson Innovative Medicine for the development and commercialization of AAV-CNGB3, AAV-CNGA3 and bota-vec, which Collaboration Agreement was terminated in December 2023 in connection with our entering into the Asset Purchase Agreement with Johnson & Johnson Innovative Medicine. In addition, in October 2023 we provided Sanofi and its affiliates with a right of first negotiation for use of our riboswitch gene regulation technology for certain Immunology and Inflammation (I&I), including modulation of IL-4 and IL-13, and Central Nervous System (CNS) targets, as well as for GLP-1 and other gut peptides for metabolic disease, and for our Phase 2 xerostomia program, under the Investment Agreement. 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 applicable protocol, legal, quality, regulatory and scientific standards, including among other things, GCP requirements for clinical trials and GLP requirements for certain preclinical studies. Our reliance on these third parties does not relieve us of our regulatory responsibilities. For example, we are conducting the Phase 2 AQUAx2 clinical trial of AAV-hAQP1 for the treatment of patients with radiation-induced xerostomia at multiple clinical trial sites in North America and the United Kingdom. If any locations terminate the clinical trial, we may 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, 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.

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 partes* review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Even if such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize the applicable product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. 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 is the subject of registrations and/or pending applications 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 or acquire additional intellectual property from third parties, and such intellectual property 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 or equipment that may require the use of additional proprietary rights held by third parties. Our product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may develop products containing our compositions and pre-existing pharmaceutical compositions. These pharmaceutical products may be covered by intellectual property rights held by others. We may be required by the FDA, 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 may need to increase or decrease the size of our organization, and we may experience difficulties in managing those organizational changes, which could disrupt our operations.

As of December 31, 2024, we had 381 employees. If we seek to expand our organization, 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 or strategic opportunities related to our assets, loss of employees and reduced productivity among remaining employees. Our 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 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 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. Alternatively, if we seek to decrease the number of employees in our organization in the future in response to adverse business events, it may lead to additional unanticipated attrition. If our future staffing is inadequate because of additional unanticipated attrition or because we failed to retain the staffing level required to accomplish our business objectives, we may be delayed or unable to continue the development of our product candidates, which could impede our ability to generate revenues and achieve or maintain profitability.

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, healthcare 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 product and clinical trial liability, employment practices liability, property, transit, 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 restrictive, 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 or manufacture commercial products for third parties, we intend to acquire insurance coverage to include, as necessary, the sale, manufacture and supply 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 directors' and officers' 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 and 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 may 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 information technology, or IT, systems, including manufacturing 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, or impede our ability to meet any third party supply obligations. 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 liabilities and the further development of our product candidates could be delayed.

In the ordinary course of our business, we, our business partners and our service providers 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. Cybersecurity threats including state-sponsored attacks, ransomware, phishing, insider threats, supply chain compromises, and vulnerabilities in cloud-based services, are increasing in frequency, sophistication, persistence and severity. Attackers, ranging from criminal organizations to nation-state actors, may target our systems for financial, competitive, or political

motives. We may also face increased cybersecurity risks due to our reliance on internet technology and by allowing some of our employees to work remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

Despite our security measures, our IT 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 or critical business information. In addition, there can be no assurance that our cybersecurity risk management program and processes, including our policies, controls or procedures, will be fully effective in protecting our systems and 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, ransomware, phishing attempts, thefts of personal, confidential, proprietary or other critical business information and other attempts at compromising our IT 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.

Risks Related to Our Ordinary Shares

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

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

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of clinical trials of our product candidates or those of our competitors;
- developments related to our existing or any future collaborations;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;

- announcements by us, our partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- the impact of any potential strategic transactions related to our assets;
- 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, recommendations by securities analysts or shifting investor perceptions;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions;
- changes in accounting principles; and
- the other factors described in this "Item 1A. Risk Factors" section and elsewhere in this Form 10-K.

In addition, the stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, when the market price of a security has been volatile, holders of that security have sometimes instituted securities class action litigation against the issuer. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If any of the holders of our ordinary shares were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our senior management would be diverted from the operation of our business. Any adverse determination in litigation could also subject us to significant liabilities. Broad market and industry factors may negatively affect the market price of our ordinary shares, 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.

We may raise additional capital pursuant to our shelf registration statement, including through our "at-the-market" offering program, or through additional public or private placements, any of which could substantially dilute the investment of our stockholders.

Sales of a substantial number of our ordinary shares in the public market could dilute your ownership interest. Pursuant to an "at-the-market" sales agreement we entered into with BofA Securities, Inc., or BofA, in December 2023, we may sell from time to time, ordinary shares having an aggregate offering price of up to $100.0 million through BofA, acting as our agent. During the year ended December 31, 2024, the Company raised gross proceeds of $8.4 million through the sale of 1,508,517 ordinary shares pursuant to an "at-the-market" equity offering program. Whether we choose to affect future sales under the "at-the-market" equity offering program will depend on a number of factors, including, among others, market conditions and the trading price of our ordinary shares relative to other sources of capital. The issuance from time to time of ordinary shares through our "at-the-market" equity offering program or in any other equity offering, or the perception that such sales may occur, could have the effect of depressing the market price of our ordinary shares.

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, 2024, 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 56.5% of our outstanding ordinary shares. In addition, in connection with entering into the Financing Agreement, we issued to an affiliate of Perceptive Advisors, LLC, our largest shareholder that employs a director serving on our board, warrants to purchase an aggregate of 700,000 of our 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 a "smaller reporting company," and the reduced disclosure requirements applicable to smaller reporting companies may make our ordinary shares less attractive to investors.

We are 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. 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 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 Act (as amended), or the Companies Act, 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, 2024, 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, 2024 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 Ireland 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, 2024, we had federal and state NOL carryforwards in the United States of $74.3 million and $19.3 million, respectively, and cumulative carryforward tax losses in the UK of $203.7 million, 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). As of December 31, 2024, cumulative carryforward tax losses in Ireland were $78.3 million. 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. U.S. federal NOLs generated prior to December 31, 2017 may only be carried forward for 20 years. As of December 31, 2024, we also had orphan drug and research and development credits in the U.S. in the amount of $22.5 million, both of which may be carried forward for 20 years and are expected to begin expiring in 2035 if not utilized. We also had research and development credits in the UK of $1.9 million, which may be carried forward indefinitely until utilized. The UK and Ireland carryforward tax losses will continue indefinitely, subject to relevant restrictions, under current jurisdictional tax law.

The NOLs and carryforward tax losses are subject to review and possible adjustment by the applicable tax authorities. Additionally, 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 and the Taxes Consolidation Act 1997 (TCA 1997) under the Ireland 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 August 2024, there were no limitations in the UK. However, for U.S. purposes, we determined that a change of ownership occurred in April 2016 and again in June 2018, but there was not a limit for utilizing these losses to offset the 2022 income. We have performed a 382 analysis through August 2024 and no additional change of ownership has occurred. 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 have received in the past or may receive in the future pursuant to existing or future equity and debt financings, including under our "at-the-market" equity offering program. 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 ability to apply certain proceeds may be restricted. For example, in August 2024, we conducted an equity financing by selling an aggregate of 12.75 million ordinary shares at a price of $4.00 per share for gross proceeds of $51.0 million. Our failure to apply any such 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 and existing compliance initiatives and corporate governance practices.

As a public company, and particularly since we no longer qualify as an emerging growth company and if we no longer qualify as a smaller reporting company or a non-accelerated filer in the future, we incur and will continue to incur significant legal, accounting and other expenses. 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 are a non-accelerated filer, 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 a non-accelerated filer, 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.

Expectations relating to environmental, social and governance factors may impose additional costs and expose us to new risks.

There is an increasing focus from the SEC, foreign regulators, stock exchanges, certain investors and other stakeholders concerning corporate responsibility, specifically related to environmental, social and governance factors. The SEC has adopted rules regarding new climate-related disclosure, which have been stayed by the SEC pending the outcome of pending litigation challenging the new rules. Some investors may use these and other environmental, social and governance factors to guide their investment strategies and, in some cases, may choose not to invest in us if they believe our policies and disclosures relating to corporate responsibility are inadequate. Third-party providers of corporate responsibility ratings and reports on companies have varied and in some cases inconsistent standards. In addition, the criteria by which companies' corporate responsibility practices are assessed are evolving, which could result in greater expectations of us and cause us to undertake costly initiatives to satisfy such new criteria. Alternatively, if we elect not to or are unable to satisfy such new criteria or do not meet the criteria of a specific third-party provider, some investors may conclude that our policies with respect to corporate responsibility are insufficient. We may face reputational damage in the event that our corporate responsibility procedures or standards do not meet the standards set by various constituencies. Furthermore, if our competitors' corporate responsibility performance is perceived to be greater than ours, potential or current investors may elect to invest with our competitors instead. In addition, in the event that we communicate or disclose certain initiatives and goals regarding environmental, social and governance matters, we could fail, or be perceived to fail, in our achievement of such initiatives or goals, or we could be criticized for the scope of such initiatives or goals or be subject to litigation for such failures. If we fail to satisfy the expectations of investors and other stakeholders or our initiatives are not executed as planned, our reputation and financial results could be adversely affected.

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. In addition, the Notes Purchase Agreement prohibits us from paying dividends during its term and the terms of existing and future financing agreements may also preclude us from paying dividends. 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 additional information.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 1C. CYBERSECURITY

Cybersecurity Risk Management and Strategy

We have implemented and maintain a cybersecurity risk management program that includes processes designed for the identification, assessment and mitigation of cybersecurity risks in order to protect the confidentiality, integrity and availability of our critical systems and information. We have designed and assessed our program based on the Center for Internet Security (CIS) Controls standard and the National Institute of Standards and Technology Cybersecurity Framework (NIST CSF).

Our cybersecurity risk management program is integrated into our overall enterprise risk management program, and includes:

- risk assessments designed to help identify material cybersecurity risks to our critical systems, information, products, services, and our broader enterprise IT environment;
- security controls and mitigation measures designed to manage and mitigate material risks from cybersecurity threats to our critical systems and information;
- an IT and security team responsible for managing (1) our cybersecurity risk assessment processes, (2) our security controls and mitigation measures, and (3) our response to cybersecurity incidents;
- the use of external service providers, where appropriate, to assess, test or otherwise assist with aspects of our security controls;
- cybersecurity awareness training of our employees, IT and security personnel and senior management;
- a cybersecurity incident response plan that includes procedures for responding to cybersecurity incidents; and
- a risk-based approach to identifying and overseeing third party cybersecurity risks, including evaluating the cybersecurity processes of service providers and other vendors, and reviewing available security certifications and independent audit reports.

Although, to our knowledge, we have not experienced any material cybersecurity breach to date, we may experience cybersecurity incidents and face risks from cybersecurity threats that, if realized, are reasonably likely to materially affect us, including our operations, business strategy, results of operations or financial condition. For more information regarding how cybersecurity risks may affect us, see "Item 1A Risk Factors."

Cybersecurity Governance

Our Board considers cybersecurity risk as part of its risk oversight function and has delegated oversight of cybersecurity and other IT risks to the Audit Committee. The Audit Committee oversees management's implementation of our cybersecurity risk management program.

The Audit Committee receives reports from management on our cybersecurity risks at least semi-annually. In addition, management updates the Audit Committee regarding cybersecurity matters, as necessary, including any material cybersecurity incidents, as well as any incidents with lesser impact potential. The Audit Committee reports to the full Board regarding its activities and the full Board periodically receives briefings from management on our cybersecurity risk management program.

Our management team is responsible for assessing and managing risks from cybersecurity threats. The Vice President, Global IT and Senior Vice President, Risk and Internal Controls have primary responsibility for our overall cybersecurity risk management program and supervise both our internal cybersecurity personnel and our external cybersecurity consultants. They provide briefings to the management team, including the Chief Financial Officer/Chief Operating Officer and the General Counsel and Secretary, as well as the Board and the Audit Committee. Their briefings include topics such as threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us. The briefings also cover alerts and reports produced by security tools deployed in our IT environment. Our Vice President, Global IT has over 20 years' experience leading teams in cybersecurity, and designing and securing critical IT infrastructure in the healthcare, biotech and sports entertainment sectors. Our Senior Vice President, Risk and Internal Controls has more than 30 years' experience designing, implementing and leading risk management, internal control and compliance programs, including cybersecurity, data privacy and business resilience, in global organizations.

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 own a long leasehold interest in the ground rights where our 29,000 square foot GMP viral vector 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. We also own the buildings housing our second, large scale GMP viral vector manufacturing facility and our first GMP plasmid and DNA production facility located in Buildings 2 and 3, Block K, Airport Avenue, Shannon Free Zone, Shannon Ireland. The Shannon campus encompasses an aggregate of 150,000 square feet. We entered into a lease for each property providing for a long leasehold interest that expires in 2211.

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

ITEM 3. LEGAL PROCEEDINGS

We are not subject to any material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

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

Market Information

Our ordinary shares trade on the Nasdaq Global Select Market under the symbol "MGTX."

Holders of Record

As of February 28, 2025, there were 51 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. In addition, the Notes Purchase Agreement prohibits us from paying dividends during its term and the terms of existing and future financing agreements may also preclude us from paying dividends. 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. [RESERVED]

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 genetic medicines company with a broad pipeline of late-stage clinical programs, including Parkinson's disease, radiation-induced xerostomia and AIPL1-associated retinal dystrophy. Our clinical programs use targeted local delivery of small doses of genetic medicines to treat both inherited and more common conditions with severe unmet need. The successful development of the clinical pipeline is supported by our internal end-to-end manufacturing capabilities. We have two GMP viral vector production facilities, internal plasmid production for GMP, as well as an in-house Quality Control hub for stability and release, all fit for IND through

commercial supply. In addition, we have developed a proprietary manufacturing platform with leading yield and quality aspects and commercial readiness. Our core capabilities in viral vector and capsid optimization allow increased potency, decreased dose and significantly reduced cost of goods for our genetic medicines. We have developed a potentially transformative gene regulation platform using bespoke synthetic riboswitch technology invented in-house that allows for the precise, dose-responsive control of any transgene under the control of oral small molecules. We are focusing the riboswitch platform on *in vivo* delivery of biologic therapeutics such as the metabolic peptides GLP-1, GIP, glucagon, amylin, PYY and leptin via oral small molecules, as well as cell therapy for oncology and autoimmune diseases, and long-term intractable pain. We have developed unique comprehensive technology capabilities to apply genetic medicine to more common diseases, increasing efficacy, addressing novel targets, and expanding access in some of the largest disease areas where the unmet need remains high.

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 our GMP plasmid and DNA production facility and developing manufacturing processes, advancing the product candidates in our ophthalmology, salivary gland and neurodegenerative disease programs, building our intellectual property portfolio, organizing and staffing our company, developing our business plan, raising capital, and providing general and administrative support for these operations. 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, debt financing and upfront and milestone payments in connection with the Collaboration Agreement and Asset Purchase Agreement. Through December 31, 2024, we received gross proceeds of approximately $622.3 million from sales of our ordinary shares, Series A ordinary shares and convertible preferred C shares, gross proceeds of approximately $75.0 million from issuance of debt, $130.0 million from the Collaboration Agreement with Johnson & Johnson Innovative Medicine, and $125.0 million from the Asset Purchase Agreement with Johnson & Johnson Innovative Medicine. As of December 31, 2024, we had cash, cash equivalents and restricted cash of $105.7 million, as well as $0.7 million we expect to receive from Johnson & Johnson Innovative Medicine in the first quarter of 2025 in connection with the PPQ and transition services we provided to Johnson & Johnson Innovative Medicine.

We are a clinical stage company and have not generated any product revenues to date. We have ongoing clinical development programs and a broad pipeline of preclinical programs. Since inception, we have incurred significant operating losses. Our net losses for the years ended December 31, 2024 and 2023 were $147.8 million and $84.0 million, respectively. As of December 31, 2024, we had an accumulated deficit of $702.0 million. We do not expect to generate revenue from sales of products unless and until we successfully initiate and complete clinical development and obtain regulatory approval for any product candidates, or satisfy our third party obligations. Under the Collaboration Agreement, we received an upfront payment in the amount of $100.0 million in March 2019 and a milestone payment in the amount of $30.0 million in December 2021. Additionally, pursuant to the Collaboration Agreement, we received research and development funding for certain research, manufacturing and clinical development costs. On December 20, 2023, we entered into an Asset Purchase Agreement with Johnson & Johnson Innovative Medicine pursuant to which the Company sold and assigned to Johnson & Johnson Innovative Medicine a License Agreement between the Company and UCLB relating to the research, development, manufacture and exploitation of the RPGR Product, and other related assets as described in the Asset Purchase Agreement. In connection with entering into the Asset Purchase Agreement, we entered into a Termination Agreement with Johnson & Johnson Innovative Medicine terminating the Collaboration Agreement. The Company and Johnson & Johnson Innovative Medicine also entered into a Supply Agreement on December 20, 2023 pursuant to which the Company agreed to manufacture and supply the RPGR Product for Johnson & Johnson Innovative Medicine. In December 2023, we received a non-refundable upfront payment of $65.0 million in connection with the Asset Purchase Agreement. During the year ended December 31, 2024, we received $60.0 million in milestone payments under the Asset Purchase Agreement.

Our total operating expenses were $197.5 million and $151.1 million for the years ended December 31, 2024 and 2023, respectively. We expect to continue incurring increasing costs associated with our clinical activities for AAV-hAQP1 for the treatment of radiation-induced xerostomia and xerostomia associated with Sjogren's syndrome, AAV-GAD for the treatment of Parkinson's disease, as well as costs associated with the delivery of services under the Asset Purchase and related agreements. We also incurred expenses during the year ended December 31, 2024 and expect to continue to incur expenses related to research activities in additional therapeutic areas to expand our pipeline, developing our potentially transformative gene regulation technology, hiring additional personnel as needed 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.

On May 3, 2023, we entered into a securities purchase agreement with certain accredited investors, pursuant to which we, in a private placement, agreed to issue and sell an aggregate of 10,773,913 ordinary shares at a purchase price of $5.75 per share, for gross proceeds of approximately $62.0 million. The closing occurred on May 5, 2023.

On October 30, 2023, we entered into the Investment Agreement with Sanofi Foreign Participations, and solely for the limited purposes set forth therein, Sanofi, pursuant to which, among other things and subject to the terms and conditions specified therein, we issued an aggregate of 4,000,000 ordinary shares of the Company at a purchase price of $7.50 per share for gross proceeds of $30.0 million. The Investment Agreement also provides Sanofi Foreign Participations and its affiliates with a right of first negotiation for use of our riboswitch gene regulation technology for certain Immunology and Inflammation (I&I), including modulation of IL-4 and IL-13, and Central Nervous System (CNS) targets, as well as for GLP-1 and other gut peptides for metabolic disease, and for our Phase 2 xerostomia program, in each case, on the terms set forth therein.

On December 20, 2023, we entered into an Asset Purchase Agreement with Johnson & Johnson Innovative Medicine pursuant to which the Company sold and assigned to Johnson & Johnson Innovative Medicine a License Agreement between the Company and UCLB relating to the research, development, manufacture and exploitation of the RPGR Product, and other related assets as described in the APA. In connection with entering into the Asset Purchase Agreement, we entered into a Termination Agreement with Johnson & Johnson Innovative Medicine terminating the Collaboration Agreement. The Company and Johnson & Johnson Innovative Medicine also entered into a Supply Agreement on December 20, 2023 pursuant to which we agreed to manufacture and supply the RPGR Product for Johnson & Johnson Innovative Medicine. Under the Asset Purchase Agreement, Johnson & Johnson Innovative Medicine paid the Company a non-refundable upfront cash payment of $65.0 million in December 2023. Additionally, pursuant to and subject to the terms and conditions set forth in the Asset Purchase Agreement, Johnson & Johnson Innovative Medicine agreed to pay the Company future contingent consideration of up to an aggregate of $350.0 million, as follows: (i) a milestone payment of $50.0 million in connection with the achievement of the initiation of the extension study for the Phase 3 LUMEOS clinical trial for the RPGR Product; (ii) $10.0 million upon completion of certain specified development services for the drug substance for the RPGR Product; (iii) $5.0 million upon completion of certain specified development services for the drug product for the RPGR Product; (iv) $175.0 million upon the first commercial sale of an RPGR Product in the United States; (v) $75.0 million upon the first commercial sale of an RPGR Product in at least one of the United Kingdom, France, Germany, Spain and Italy; (vi) $25.0 million upon completion of the transfer of certain manufacturing technology for drug substance and drug product from the Company to Johnson & Johnson Innovative Medicine; and (vii) $10.0 million upon regulatory approval of a Johnson & Johnson Innovative Medicine-selected manufacturing facility in each of the United States and European Union for commercial manufacture of the RPGR Product. As of December 31, 2024, we have received $60.0 million in milestone payments from Johnson & Johnson Innovative Medicine. Johnson & Johnson Innovative Medicine is also responsible for any royalty or milestone amounts that become payable on the RPGR Product under the UCLB RPGR License Agreement.

In December 2023, we entered into an "at-the-market" sales agreement with BofA Securities, Inc., or BofA, pursuant to which we may sell from time to time, ordinary shares having an aggregate offering price of up to $100.0 million through BofA, acting as our agent. During the year ended December 31, 2024, we raised gross proceeds of $8.4

million through the sale of 1,508,517 ordinary shares pursuant to an "at-the-market" equity offering program. Under the "at-the-market" equity program which is currently effective and may remain available for us to use in the future, we may sell an additional $91.6 million of ordinary shares. Whether we choose to affect future sales under the "at-the-market" equity offering program will depend on a number of factors, including, among others, market conditions and the trading price of our ordinary shares relative to other sources of capital.

On August 12, 2024, we entered into an underwriting agreement with BofA in connection with the issuance and sale by the Company in a public offering of 12,500,000 of our ordinary shares at a public offering price of $4.00 per share, less underwriting discounts and commissions, pursuant to an effective shelf registration statement on Form S-3 (Registration No. 333-276183) and a related prospectus supplement filed with the SEC. The closing of the offering occurred on August 13, 2024. We received gross proceeds from the offering of $50.0 million and incurred underwriting discounts and commissions and estimated offering expenses of approximately $1.9 million.

On August 12, 2024, the Company agreed to sell shares to an accredited investor (the "Investor") through a private placement rather than through the public offering and as a result, on August 23, 2024, we entered into a securities purchase agreement with the Investor, pursuant to which we, in a private placement, agreed to issue and sell to the Investor 250,000 ordinary shares at a purchase price of $4.00 per share, for gross proceeds of $1.0 million (the "Private Placement"). The closing of the Private Placement occurred on August 29, 2024.

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, cash equivalents, accounts receivable – related party and tax incentive receivable at December 31, 2024, together with the proceeds from the anticipated closing of the strategic collaboration with Hologen Ltd, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into 2027 and to repay our debt obligation of $75.0 million to Perceptive (due in August 2026). This estimate does not include the $285.0 million in milestones we are eligible to receive under the Asset Purchase Agreement upon first commercial sale of an RPGR Product in the United States and in at least one of the United Kingdom, France, Germany, Spain and Italy, for completion of the transfer of certain manufacturing technology to Johnson & Johnson Innovative Medicine and upon regulatory approval of a Johnson & Johnson Innovative Medicine-selected manufacturing facility in each of the United States and European Union for commercial manufacture of the RPGR Product. 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

Strategic Collaboration with Hologen AI:

- We will receive $200 million in upfront cash consideration at closing.
- We and Hologen will form a joint venture, Hologen Neuro AI Ltd, with additional committed funding from Hologen of up to $230 million into the joint venture to finance the development of the AAV-GAD program in Parkinson's disease to commercialization, as well as other locally-delivered therapies to the CNS.
- The joint venture, Hologen Neuro AI Ltd, will use Hologen's proprietary multi-modal generative foundation models (LMMs).
- We will hold a 30% ownership in the joint venture and will lead all clinical development and manufacturing.
- Hologen Neuro AI Ltd will enter into both clinical and commercial manufacturing supply agreements with us for exclusive manufacturing of AAV-GAD and other locally-delivered genetic medicines targeting the CNS.
- Hologen will own a minority stake in our manufacturing subsidiary and will contribute a portion of the annual funding and deploy Hologen's world leading generative AI capabilities to further accelerate the optimization of our proprietary manufacturing capabilities.

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

- Announced positive data in October 2024 from randomized, sham-controlled clinical bridging study of AAV-GAD for the treatment of Parkinson's disease.
- The primary study objective of safety and tolerability was met.
- Significant and clinically meaningful improvements from baseline demonstrated for key efficacy endpoints at 26 weeks.
- Significant improvement of 18 points in Unified Parkinson's Disease Rating Scale (UPDRS) Part 3 in the high dose group at 26 weeks (p=0.03).
- Significant improvement in the Parkinson's Disease Questionnaire (PDQ-39) score, a key quality of life measure, for both the high and low dose groups at 26 weeks.

AAV2-hAQP1 for the Treatment of Xerostomia:

- In December 2024, we were granted RMAT Designation by the FDA for AAV2-hAQP1 for the treatment of Grade 2/3 RIX.
- RMAT designation includes the benefits of the Fast Track and Breakthrough Therapy designations, allows frequent regulatory interactions with the FDA, and potential routes to accelerated approval and Priority Review.

- We have gained alignment with the FDA on requirements for the ongoing Phase 2 AQUAx2 clinical trial for Grade 2/3 RIX to be considered a pivotal trial in support of a potential BLA filing based on the use of material manufactured using our proprietary production process and in-house manufacturing.
- Data from our Phase 1 AQUAx clinical trial were presented in an oral session at the American Academy of Oral Medicine (AAOM) 2024 annual meeting in April 2024, demonstrating that treatment with AAV2-hAQP1 resulted in significant improvements across three different patient-reported outcomes and in saliva production, with no treatment-related serious adverse events or dose-limiting toxicities reported. These data underpinned this successful RMAT designation.
- The Phase 2 AQUAx2 (NCT05926765) randomized, double-blind, placebo-controlled study continues to enroll and dose participants at multiple sites in the U.S., Canada and the U.K.
- The RMAT designation will allow us to benefit from increased interactions with the FDA to further accelerate the development pathway and potential BLA filing based on data from the ongoing pivotal study in 2026.

AAV-AIPL1 Specials License in the UK:

- In February 2025, we announced that data demonstrating the efficacy of rAAV8.*hRKp.AIPL1* for the treatment of LCA4 were published in *The Lancet* in a paper titled, "*Gene therapy in children with AIPL1-associated severe retinal dystrophy: an open-label, first-in-human interventional study*".
- As disclosed in the paper, 4 out of 4 young children with the AIPL1-associated retinal dystrophy, LCA4, benefited substantially from unilateral subretinal administration of rAAV8.hRKp.*AIPL1* with improved visual acuity, functional vision, and protection against progressive retinal degeneration.
- Following the strong safety and substantial efficacy demonstrated in this first cohort of 4 children treated unilaterally, a further 7 children were treated bilaterally, and all showed substantial benefit from treatment with rAAV8.*hRKp.AIPL1*.
- Meaningful responses were observed in 11 out of 11 LCA4 children treated to date with rAAV8.*hRKp.AIPL1*.
- Following recent meetings with the MHRA, we intend to submit a Marketing Authorization Application (MAA) under exceptional circumstances for rAAV8.*hRKp.AIPL1* based on the results from the 11 treated children with no further clinical data required.
- We have aligned on an expedited CMC package to support approval.
- We are also currently engaging with the FDA to discuss a parallel path forward for expedited approval in the U.S., as well as other global regulatory agencies.
- The Offices of Orphan Products Development and Pediatric Therapeutics of the FDA has granted RPDD to AAV8-RK-AIPL1 for the treatment of LCA4 retinal dystrophy.
- In addition, three of our other IRD programs gained RPDD: AAV8-RK-BBS10 for the treatment of Bardet-Biedl syndrome (BBS) due to BBS10 mutations; AAV5-RDH12 for the treatment of RDH12 associated retinal dystrophy; and AAV8-RK-RetGC for the treatment of Leber congenital amaurosis due to GUCY2D mutations.

An RPDD may be granted by the FDA to drugs and biologics intended to treat certain orphan diseases affecting fewer than 200,000 patients in the U.S., the serious or life-threatening manifestations of which primarily affect individuals aged 18 years or younger. Under the FDA's Rare Pediatric Disease Priority Review Voucher (PRV) program, a sponsor that receives approval for a biologics license application for a rare pediatric disease may be eligible to receive a voucher for a priority review of a subsequent marketing application for a different product. PRVs may be used by the sponsor or sold to another sponsor for their use and have recently been sold for between $100 million to $158 million.

Botaretigene Sparoparvovec for the Treatment of XLRP:

- Data from the Phase 3 LUMEOS trial of botaretigene sparoparvovec (bota-vec) for the treatment of X-linked retinitis pigmentosa in collaboration with Johnson & Johnson Innovative Medicine is expected in 2025. We are eligible to receive up to $285 million upon the first commercial sales of bota-vec in the U.S. and EU and manufacturing tech transfer.

- We also entered into a commercial supply agreement with Johnson & Johnson Innovative Medicine for bota-vec manufacturing, which we anticipate will generate additional revenue during the product launch.

Riboswitch Gene Regulation Technology Platform for *in vivo* Delivery:

- We continue to progress our riboswitch technology platform in multiple potential indications, with an initial focus on obesity and metabolic disease and CAR-T for oncology and autoimmune disease.
- We continue to generate compelling preclinical data with metabolic peptides and hormones, including incretins, myokines and leptin, which suggests greater efficacy on weight loss as well as a positive impact on fat to muscle ratio with certain novel combinations of peptides.
- Preclinical data mentioned above as well as new data on chronic pain therapies is informing the decision for our first INDs using our riboswitch small molecule platform.
- We are in dialogue with regulatory agencies and intend to initiate first-in-human studies using the riboswitch platform in 2025.

Manufacturing:

United Kingdom (MeiraGTx UK II Ltd.)

Our UK manufacturing facility holds two authorizations issued by the MHRA:

- MIA(IMP) Licence (MIA(IMP) 45522) – Authorizing manufacturing, fill-finish, and QC testing of Investigational Medicinal Products (IMPs).

- Specials Licence (MS 45522) – Authorizing manufacturing, fill-finish, and QC testing of 'Special' medicinal products.

The UK facility was inspected in May 2024, and the licences were successfully renewed. The outcome of this inspection confirmed that the site was found to be in compliance with GMP requirements for Investigational Medicinal Products (IMPs) and was operating at the required compliance level to support an application for a commercial MIA licence. We plan to submit this application in the second quarter of 2025.

Ireland (MeiraGTx Ireland DAC)

Our Shannon facility holds two authorizations issued by Ireland's Health Products Regulatory Authority (HPRA):

- MIA Licence (M1316) – Authorizing QC testing of commercial products (awarded June 2023).
- MIA(IMP) Licence (IMP13221) – Authorizing QC testing of Investigational Medicinal Products (IMPs) (awarded September 2023/QC and 2025/MFG).

The QC laboratory is actively undertaking release and stability testing on PPQ batches.

The latest HPRA inspection in February 2025 was highly successful—both QC licences were renewed, and viral vector manufacturing was added to the MIA(IMP) licence. This means the Shannon site can manufacture material for use in clinical trials, a first-of-its-kind licence for a gene therapy facility in Ireland.

Strategic Investment from Sanofi:

- On August 12, 2024, Sanofi purchased $30 million of ordinary shares of the Company.
- Sanofi holds a right of first negotiation (ROFN) for the use of our riboswitch gene regulation technology for certain Central Nervous System (CNS) and Immunology and Inflammation (I&I) targets, including IL-4 and IL-13, as well as for GLP-1 and other gut peptides for obesity, and for our Phase 2 xerostomia program.

Components of Our Results of Operations

Service Revenue – Related Party

Our service revenue consisted of the process performance qualification ("PPQ") services performed in connection with the Asset Purchase Agreement and related agreements.

License Revenue – Related Party

Our license revenue consisted of the amortization of the upfront and milestone payments 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. Beginning in 2024, we incurred expenses classified as cost of service revenue – related party performed in connection with the Asset Purchase Agreement and related agreements.

Cost of Service Revenue – Related Party

Our cost of service revenue consisted of the PPQ services performed in connection with the Asset Purchase Agreement and related agreements.

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 have 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; maintaining and protecting our intellectual property portfolio; 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 and impairment 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 to continue incurring increasing research and development costs associated with our clinical activities for AAV-hAQP1 for the treatment of radiation-induced xerostomia and xerostomia associated with Sjogren's syndrome, as well as for AAV-GAD for the treatment of Parkinson's disease. In addition, we expect to continue to incur expenses related to research activities in additional therapeutic areas to expand our pipeline and develop our potentially transformative gene regulation technology.

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 are measured using the foreign subsidiaries' local currency as the functional currency, either the pound sterling or the euro. 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.

Interest Income

Interest income is comprised on interest earned on our interest-bearing bank accounts.

Interest Expense

Interest expense consists of interest expense and amortization of the debt discount in connection with the debt financing described in Note 13 to our consolidated financial statements.

Gain on Sale of Nonfinancial Assets

The gain on sale of nonfinancial assets represents the value allocated to the nonfinancial assets sold and assigned to Johnson & Johnson Innovative Medicine including the UCLB RPGR License Agreement relating to the research, development, manufacture and exploitation of the RPGR Product, and other related assets pursuant to the Asset Purchase Agreement, net of carrying value.

Other Comprehensive Loss

Other comprehensive loss includes the following:

Foreign Currency Translation Loss

Expenses of 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 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.

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.

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 we conclude that some or all aspects of the arrangement are within the scope of ASC 808 and do not represent a transaction with a customer, we recognize our allocation of the shared costs incurred with respect to the jointly conducted activities pursuant to ASC 730, *Research and Development* ("ASC 730"). If we concluded that some or all aspects of the arrangement represent a transaction with a customer, we account for those aspects of the arrangement within the scope of ASC 606. 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

We evaluate the promised goods or services to determine which promises, or group of promises, represent performance obligations in our contracts with customers. 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.

At inception, we determine whether contracts are within the scope of ASC 606 or other topics. For contracts that are determined to be within the scope of 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, 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, 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.

If there are multiple performance obligations, we allocate the transaction price to each performance obligation based on their estimated standalone selling prices ("SSP"). We estimate the SSP for each performance obligation by considering information such as market conditions, entity-specific factors, and information about our customer that is reasonably available. We consider estimation approaches that allow us to maximize the use of observable inputs. These estimation approaches may include the adjusted market assessment approach, the expected cost plus a margin approach or the residual approach. We also consider whether to use a different estimation approach or a combination of approaches to estimate the SSP for each performance obligation. Developing certain assumptions (e.g., treatable patient population, expected market share, probability of success and product profitability, and discount rate based on weighted-average cost of capital) to estimate the SSP of a performance obligation requires significant judgment.

We record amounts as contract assets when the right to consideration is deemed unconditional. Contract assets are reclassified as accounts receivable once billed. 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.

Our collaboration and 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, we recognize 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, 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 for purposes of recognizing revenue from non-refundable, up-front fees. We evaluate 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, we evaluate each milestone to determine when and how much of the milestone to include in the transaction price. We first estimate the amount of the milestone payment that we could receive using either the expected value or the most likely amount approach. We primarily use the most likely amount approach as that approach is generally most predictive for milestone payments with a binary outcome. Then, we consider 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.) We update 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, we 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, we have not recognized any revenue related to sales-based royalties or milestone payments based on the level of sales.

Research and Development Services: Under the Collaboration Agreement, we incurred research and development costs, with Johnson & Johnson Innovative Medicine responsible for up to 100% of the costs, depending on the type of research and development services being performed. We recorded costs associated with the development activities as research and development expenses in the consolidated statements of operations and comprehensive loss consistent with ASC 730. The reimbursement of the research and development costs by Johnson & Johnson Innovative Medicine was representative of the joint risk sharing nature of the arrangement. We considered the guidance in ASC 808 and recognize the payments received from Johnson & Johnson Innovative Medicine as a reduction to research and development expense when the related costs are incurred. Under the Asset Purchase Agreement, research and development services (PPQ services) are recorded as incurred under cost of service revenue – related party.

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the customer's discretion are generally considered options. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations at the outset of the arrangement.

Customer Options: Customer options are evaluated at contract inception to determine whether those options provide a material right (i.e., an optional good or service offered for free or at a discount) to the customer. If the customer options represent a material right, the material right is treated as a separate performance obligation at the outset of the arrangement. We allocate the transaction price to material rights based on the standalone selling price. As a practical alternative to estimating the standalone selling price of a material right when the underlying goods or services are both (i) similar to the original goods or services in the contract and (ii) provided in accordance with the terms of the

original contract, we allocate the total amount of consideration expected to be received from the customer to the total goods or services expected to be provided to the customer. Amounts allocated to any material right are recognized as revenue when or as the related future goods or services are transferred or when the option expires.

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. Share-based compensation are accounted for in accordance with ASC 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all share-based payments, 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 recipients 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.

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 our Company's option grants under the SEC Staff Accounting Bulletin No. 107 and No. 110, *Share-Based Payment*.

Expected volatility is based on an analysis of our Company and 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, non-employee members of our board of directors and non-employee consultants as compensation for services performed. Awards of RSUs are accounted for in accordance with ASC 718. ASC 718 requires all share-based payments, 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.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

	2024	2023	Change
		(in thousands)	
Revenues:			
Service revenue - related party	$ 33,279	$ —	$ 33,279
License revenue - related party	—	14,017	(14,017)
Total revenue	33,279	14,017	19,262
Operating expenses:			
Cost of service revenue - related party	23,791	—	23,791
General and administrative	54,216	47,293	6,923
Research and development	119,484	103,785	15,699
Total operating expenses	197,491	151,078	46,413
Loss from operations	(164,212)	(137,061)	(27,151)
Other non-operating income (expense)			
Foreign currency (loss) gain	(2,886)	9,300	(12,186)
Interest income	4,145	2,272	1,873
Interest expense	(13,272)	(13,245)	(27)
Gain on sale of nonfinancial assets	28,434	54,208	(25,774)
Fair value adjustments	—	499	(499)
Net loss	$ (147,791)	$ (84,027)	$ (63,764)
Other comprehensive loss:			
Foreign currency translation loss	(2,284)	(7,482)	5,198
Comprehensive loss	$ (150,075)	$ (91,509)	$ (58,566)

Service Revenue – Related Party

Service revenue was $33.3 million for the year ended December 31, 2024, due to progress of PPQ services under the Asset Purchase Agreement and related agreements. There was no service revenue for the year ended December 31, 2023.

License Revenue – Related Party

There was no license revenue for the year ended December 31, 2024, compared to $14.0 million for the year ended December 31, 2023. The decrease is due to the termination of the Collaboration Agreement concurrent with the execution of the Asset Purchase Agreement.

Cost of Service Revenue – Related Party

Cost of service revenue was $23.8 million for the year ended December 31, 2024, due to progress of PPQ services under the Asset Purchase Agreement and related agreements. There was no cost of service revenue for the year ended December 31, 2023.

General and Administrative Expenses

General and administrative expenses were $54.2 million for the year ended December 31, 2024, compared to $47.3 million for the year ended December 31, 2023. The increase of $6.9 million was primarily due to an increase of $2.1 million in professional fees, and the remaining $4.8 million was related to other general and administrative costs, none of which were individually significant.

Research and Development Expenses

Research and development expenses for the years ended December 31, 2024 and 2023 were as follows (in thousands):

	For the Years Ended December 31,		
	2024	2023	Change
Clinical Programs			
Botaretigene sparoparvovec	$ 1,250	$ 55,518	$ (54,268)
AAV-hAQP1	17,307	15,772	1,535
AAV-CNGB3 / AAV-CNGA3	(969)	2,184	(3,153)
AAV-GAD	6,411	7,598	(1,187)
Other ocular diseases	1,763	—	1,763
Manufacturing	53,445	50,221	3,224
Preclinical Programs			
Gene regulation	10,509	8,324	2,185
Neurodegenerative diseases	1,608	2,242	(634)
Preclinical ocular diseases	2,474	2,849	(375)
Other research and development expenses	25,686	29,506	(3,820)
Gross research and development expenses	119,484	174,214	(54,730)
Johnson & Johnson Innovative Medicine reimbursement	—	(70,429)	70,429
Research and development expenses	$ 119,484	$ 103,785	$ 15,699

Clinical program expenses represent the direct costs for each clinical trial plus the cost of the clinical trial material charged from the manufacturing costs.

Manufacturing expenses represent the costs to manufacture clinical trial material, including payroll, facilities, manufacturing supplies, raw materials, quality control and quality assurance. Upon completion of the manufacture of a batch of clinical trial material, the standard cost of manufacturing the batch of clinical trial material is charged to the clinical programs.

Preclinical program expenses represent the direct costs for each group of preclinical programs.

Other research and development expenses represent costs that are not allocated to a specific clinical or preclinical program, such as payroll and payroll related costs, share-based compensation, travel, rent and facilities costs, depreciation and other non-program specific expenses.

Research and development expenses for the year ended December 31, 2024 were $119.5 million, compared to $103.8 million for the year ended December 31, 2023. The increase of $15.7 million was primarily due to an increase in manufacturing costs of $3.2 million, preclinical expenses of $1.2 million and a reduction in reimbursements from Johnson & Johnson Innovative Medicine of $70.4 million as the reimbursement for the year ended December 31, 2023 was in connection with research funding provided under the Collaboration Agreement, which was terminated on

December 20, 2023. These increases were partially offset by a decrease of $55.3 million in clinical trial expenses primarily related to bota-vec as Johnson & Johnson Innovative Medicine is now primarily funding the research and development related to this program as a result of the Asset Purchase Agreement and $3.8 million of other research and development expenses.

Foreign Currency (Loss) Gain

Foreign currency loss was $2.9 million for the year ended December 31, 2024 compared to a gain of $9.3 million for the year ended December 31, 2023. The change of $12.2 million was primarily due to the restructuring and payment of certain intercompany receivables and payables during the year ended December 31, 2023. Foreign currency gains and losses subsequent to the restructuring are recorded as a part of accumulated other comprehensive income.

Interest Income

Interest income was $4.1 million for the year ended December 31, 2024 compared to $2.3 million for the year ended December 31, 2023. The increase was due to higher interest rates and cash balances during 2024.

Interest Expense

Interest expense was $13.3 million for each of the years ended December 31, 2024 and 2023.

Gain on Sale of Nonfinancial Assets

The gain on sale of nonfinancial assets was $28.4 million for the year ended December 31, 2024 compared to $54.2 million for the year ended December 31, 2023. This decrease was a result of a lower value of transaction consideration recognized in connection with the Asset Purchase Agreement during the year ended December 31, 2024 compared to the year ended December 31, 2023.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. For the year ended December 31, 2024, we used $104.5 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 as well as to manufacture commercial products, expanding our intellectual property portfolio, and providing general and administrative support for our operations. As a result of these incurred and expected expenses we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements, or other sources.

We do not currently have any approved products and have never generated any revenue from product sales. We have historically financed our operations primarily through cash on hand and proceeds from the sale of our ordinary shares, series A ordinary shares and convertible preferred C shares and upfront and milestone payments from collaboration agreements. On December 20, 2023, we entered into an Asset Purchase Agreement with Johnson & Johnson Innovative Medicine pursuant to which the Company sold and assigned to Johnson & Johnson Innovative Medicine a License Agreement between the Company and UCLB relating to the research, development, manufacture and exploitation of the RPGR Product, and other related assets as described in the Asset Purchase Agreement. In connection with entering into the Asset Purchase Agreement, we entered into a Termination Agreement with Johnson &

Johnson Innovative Medicine terminating the Collaboration Agreement. The Company and Johnson & Johnson Innovative Medicine also entered into a Supply Agreement on December 20, 2023 pursuant to which the Company agreed to manufacture and supply the RPGR Product for Johnson & Johnson Innovative Medicine. During the year ended December 31, 2024, we received $60.0 million in milestone payments under the Asset Purchase Agreement.

Additionally, on August 2, 2022, we, as borrower, and our Subsidiary Guarantors, entered into a Financing Agreement by and among us, the Subsidiary Guarantors, the lenders and other parties from time to time party thereto and Perceptive, as administrative agent and lender. On December 19, 2022, the Financing Agreement was converted to a Notes Purchase Agreement between the same parties and under substantially the same terms and conditions as the Financing Agreement, subject to certain customary note constitution terms.

The Notes Purchase Agreement provides for the issuance of the Tranche 1 Notes in an initial amount of $75.0 million. Pursuant to the First Consent and Amendment, we were able to request, in our sole discretion, and Perceptive agreed to subscribe to purchase upon such request, the issuance of the Tranche 2 Notes in an additional amount of $25.0 million at any time before August 2, 2024 subject to the terms of the Notes Purchase Agreement. Previously, our request for the issuance of the Tranche 2 Notes was to be determined at Perceptive's sole discretion. The Notes Purchase Agreement matures on August 2, 2026 and is interest-only during the term. We have the option to redeem outstanding principal notes at any time along with an applicable early redemption fee. Under each of the First Consent and Amendment and the Second Consent and Amendment, the Notes Purchase Agreement was amended to increase the applicable early redemption fee. Outstanding amounts under the Notes Purchase Agreement bear interest at a fluctuating rate per annum equal to 10.00% plus the secured overnight financing rate administered by the Federal Reserve Bank of New York for a one-month tenor, subject to a 1.00% floor.

Our obligations under the Notes Purchase Agreement are secured by our London, UK and Shannon, Ireland manufacturing facilities, $3.0 million of our cash and the bank accounts of the Subsidiary Guarantors, and the issued and outstanding equity interests of the Subsidiary Guarantors.

The Notes Purchase Agreement imposes certain covenants and restrictions on us and the Subsidiary Guarantors, including restrictions pertaining to: (i) the incurrence of additional indebtedness, (ii) limitations on liens, (iii) limitations on certain investments, (iv) making distributions, dividends and other payments, (v) mergers, consolidations and acquisitions, (vi) dispositions of assets, (vii) our maintenance of at least $3.0 million in a U.S. bank account, (viii) transactions with affiliates, (ix) changes to governing documents, (x) changes to certain agreements and leases and (xi) changes in control; however, certain of these restrictions contain exceptions which allow us to license, sell and monetize assets in our AAV-hAQP1 program in development to treat radiation-induced xerostomia, our AAV-GAD program in development to treat Parkinson's disease and our gene regulation platform technologies.

In connection with entering into the Financing Agreement, we granted warrants (the "Warrants") to Perceptive to purchase up to (i) 400,000 ordinary shares of the Company at an exercise price of $15.00 per share and (ii) 300,000 ordinary shares of the Company at an exercise price of $20.00 per share. The Warrants will expire on August 2, 2027.

Based on our current cash, cash equivalents, accounts receivable – related party, and tax incentive receivable at December 31, 2024, together with the proceeds from the anticipated closing of the strategic collaboration with Hologen Ltd, we estimate that we will be able to fund our operating expenses and capital expenditure requirements into 2027 and to repay our debt obligation of $75.0 million to Perceptive (due in August 2026). This estimate does not include the $285.0 million in milestones we are eligible to receive under the Asset Purchase Agreement upon first commercial sale of an RPGR Product in the United States and in at least one of the United Kingdom, France, Germany, Spain and Italy, for completion of the transfer of certain manufacturing technology to Johnson & Johnson Innovative Medicine and upon regulatory approval of a Johnson & Johnson Innovative Medicine-selected manufacturing facility in each of the United States and European Union for commercial manufacture of the RPGR Product. 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 $105.7 million and $130.6 million of cash, cash equivalents, and restricted cash as of December 31, 2024 and 2023, respectively.

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

	For the Years Ended December 31,	
	2024	2023
	(in thousands)	
Net cash used in operating activities	$ (104,495)	$ (105,365)
Net cash provided by investing activities	23,479	34,034
Net cash provided by financing activities	54,534	84,023
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (26,482)	$ 12,692

Operating Activities

During the year ended December 31, 2024, our cash used in operating activities of $104.5 million was primarily due to our net loss of $147.8 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 net non-cash income and expense of $13.6 million, which consisted primarily of $25.2 million of share-based compensation, $12.8 million of depreciation and amortization, $2.9 million of a foreign currency loss and $1.3 million of non-cash interest, which was partially offset by $28.4 million of a gain on sale of nonfinancial assets and $0.2 million of a gain on termination of lease liabilities. Additionally, operating assets, consisting of accounts receivable – related party, contract assets – related party, prepaid expenses, tax incentive receivable, other current assets, inventory and other assets, net, decreased by $6.2 million and operating liabilities, consisting of accounts payable, accrued expenses, other current liabilities and deferred revenue – related party, increased by $23.5 million.

During the year ended December 31, 2023, our cash used in operating activities of $105.4 million was primarily due to our net loss of $84.0 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 net non-cash income and expense of $20.4 million, which consisted primarily of $27.7 million of share-based compensation, $13.7 million of depreciation and amortization, $1.3 million of non-cash interest and $1.1 million impairment related to acquired in-process research and development, which was partially offset by $54.2 million of a gain on sale of nonfinancial assets, $9.3 million of a foreign currency gain, $0.5 million of a fair value upward adjustment and $0.2 million of net change in right-of-use assets and liabilities. Additionally, operating assets, consisting of accounts receivable – related party, prepaid expenses, tax incentive receivable, other current assets and other assets, net, decreased by $6.0 million and operating liabilities, consisting of accounts payable, accrued expenses, other current liabilities and deferred revenue – related party, decreased by $6.9 million.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2024 of $23.5 million consisted of $28.4 million from proceeds from the sale of nonfinancial assets offset by $4.9 million of purchases of property and equipment for our manufacturing, laboratory and process development facilities.

Net cash provided by investing activities for the year ended December 31, 2023 of $34.0 million consisted of $54.2 million from proceeds from the sale of nonfinancial assets offset by $20.2 million of purchases of property and equipment for our manufacturing, laboratory and process development facilities.

Financing Activities

Net cash provided by financing activities was $54.5 million for the year ended December 31, 2024, which consisted primarily of $59.4 million from the issuance of ordinary shares, which was offset by $2.5 million of issuance costs and $2.3 million of payments for withholdings of shares for income taxes.

Net cash provided by financing activities was $84.0 million for the year ended December 31, 2023, which consisted primarily of $92.0 million from the issuance of ordinary shares, which was offset by $6.4 million of issuance costs and $1.5 million of payments for withholdings of shares for income taxes.

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.

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.

Foreign Currency Exchange Risk

We currently operate in the United States, the United Kingdom and the European Union. Our activities in these jurisdictions 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. As of December 31, 2024, we did not hold any foreign currency forward contracts. With respect to our foreign currency exposures as of December 31, 2024, we estimate a 10% unfavorable movement in foreign currency exchange rates would have the effect of creating an additional foreign currency loss of approximately $11.3 million within other non-operating income (expense) for the year ended December 31, 2024.

Interest Rate Risk

We are exposed to market risk as a result of changes in interest rates applicable to borrowings under our Notes Purchase Agreement. Borrowings under the Notes Purchase Agreement bear interest at a fluctuating rate per annum equal to 10.00% plus the secured overnight financing rate ("SOFR") administered by the Federal Reserve Bank of New York for a one-month tenor, subject to a 1.00% floor. See Note 13 to our consolidated financial statements included elsewhere in this Form 10-K. We may use interest rate cap derivatives, interest rate swaps or other interest rate hedging instruments to economically hedge and manage interest rate risk with respect to our variable floating rate debt. As of December 31, 2024, the annual interest rate was 14.85% and the outstanding balance of the Tranche 1 Notes was $75.0 million. Assuming no change in the outstanding borrowings under the Notes Purchase Agreement, we estimate that a hypothetical 1% increase in the SOFR would increase our annual interest expense by approximately $0.8 million for the year ended December 31, 2024.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
FOR THE YEARS ENDED DECEMBER 31, 2024 AND 2023
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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, 2024 and 2023, 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, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024, 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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the account or disclosures to which they relate.

Accrued Clinical Trial Costs

Description of the Matter	As discussed in Note 2 to the consolidated financial statements, the Company records costs for clinical trial activities based upon estimates of costs incurred through the balance sheet date that have yet to be invoiced by the contract research organizations and other vendors. Auditing the Company's accruals for clinical trial costs is challenging due to the fact that information necessary to estimate the accruals is accumulated from multiple sources. In addition, in certain circumstances, the estimate of services that have been incurred during the reporting period requires judgment because the timing and pattern of vendor invoicing does not correspond to the level of services provided and there may be delays in invoicing from clinical study sites and other vendors.
How We Addressed the Matter in Our Audit	To test the accrued clinical trial costs, our audit procedures included, among others, testing the completeness and accuracy of the underlying data used in the estimates and evaluating the significant assumptions including, but not limited to, patient enrollment and costs per patient, and rate of progress, which are used by management to estimate the recorded accruals. To assess the reasonableness of the significant assumptions, we corroborated the progress of clinical trials with the Company's clinical team and obtained information directly from third parties related to active patient progress and currently enrolled patients. We also tested subsequent invoices received from such third parties and inspected the Company's contracts with third parties and any pending change orders to assess the costs per patient and impact to the accrual through the balance sheet date.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2016.
Jericho, New York
March 13, 2025

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	December 31, 2024	December 31, 2023
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 103,659	$ 129,566
Accounts receivable - related party	707	10,138
Contract assets - related party	950	—
Inventory	385	—
Prepaid expenses	6,828	5,625
Tax incentive receivable	8,971	13,277
Other current assets	2,018	1,016
Total Current Assets	123,518	159,622
Property, plant and equipment, net	102,878	115,896
Intangible assets, net	821	1,118
Restricted cash	2,009	1,083
Other assets	1,002	1,917
Equity method and other investments	6,749	6,766
Right-of-use assets - operating leases, net	10,576	15,910
Right-of-use assets - finance leases, net	22,198	24,432
TOTAL ASSETS	$ 269,751	$ 326,744
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 23,586	$ 16,042
Accrued expenses	27,414	42,639
Lease obligations, current	4,053	4,193
Deferred revenue - related party, current	4,827	2,926
Other current liabilities	903	1,278
Total Current Liabilities	60,783	67,078
Deferred revenue - related party	57,576	34,017
Lease obligations	7,523	12,952
Asset retirement obligations	2,821	2,401
Note payable, net	73,221	72,119
TOTAL LIABILITIES	201,924	188,567
COMMITMENTS AND CONTINGENCIES (Note 14)		
SHAREHOLDERS' EQUITY:		
Ordinary Shares, $0.00003881 par value, 1,288,327,750 authorized, 78,397,380 and 63,601,015 shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively	3	2
Capital in excess of par value	773,565	693,841
Accumulated other comprehensive loss	(3,719)	(1,435)
Accumulated deficit	(702,022)	(554,231)
Total Shareholders' Equity	67,827	138,177
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	$ 269,751	$ 326,744

See Notes to Consolidated Financial Statements

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share amounts)

	For the Years Ended December 31,	
	2024	2023
Revenues:		
Service revenue - related party	$ 33,279	$ —
License revenue - related party	—	14,017
Total revenue	33,279	14,017
Operating expenses:		
Cost of service revenue - related party	23,791	—
General and administrative	54,216	47,293
Research and development	119,484	103,785
Total operating expenses	197,491	151,078
Loss from operations	(164,212)	(137,061)
Other non-operating income (expense):		
Foreign currency (loss) gain	(2,886)	9,300
Interest income	4,145	2,272
Interest expense	(13,272)	(13,245)
Gain on sale of nonfinancial assets	28,434	54,208
Fair value adjustment	—	499
Net loss	(147,791)	(84,027)
Other comprehensive loss:		
Foreign currency translation loss	(2,284)	(7,482)
Comprehensive loss	$ (150,075)	$ (91,509)
Net loss	$ (147,791)	$ (84,027)
Basic and diluted net loss per ordinary share	$ (2.12)	$ (1.49)
Weighted-average number of ordinary shares outstanding	69,822,353	56,486,525

See Notes to Consolidated Financial Statements

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
FOR THE YEARS ENDED DECEMBER 31, 2024 AND 2023
(in thousands, except share amounts)

	Ordinary Shares	Amount	Capital in Excess of Par Value	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Equity
Balance at December 31, 2022	48,477,209	$ 2	$ 581,893	$ 6,047	$ (470,204)	$ 117,738
Share-based compensation activity	309,755	—	26,207	—	—	26,207
Issuance of shares in connection with asset acquisitions	40,138	—	209	—	—	209
Issuance of shares in connection with private placements	14,773,913	—	91,950	—	—	91,950
Issuance costs in connection with private placement	—	—	(6,418)	—	—	(6,418)
Other comprehensive loss	—	—	—	(7,482)	—	(7,482)
Net loss for the year ended December 31, 2023	—	—	—	—	(84,027)	(84,027)
Balance at December 31, 2023	63,601,015	2	693,841	(1,435)	(554,231)	138,177
Share-based compensation activity	537,848	—	22,851	—	—	22,851
Issuance of ordinary shares in at-the-market offering	1,508,517	—	8,390	—	—	8,390
Issuance costs in connection with ordinary shares	—	—	(657)	—	—	(657)
Issuance of shares in connection with registered offering	12,500,000	1	49,999	—	—	50,000
Issuance costs in connection with registered offering	—	—	(1,859)	—	—	(1,859)
Issuance of shares in connection with private placement	250,000	—	1,000	—	—	1,000
Other comprehensive loss	—	—	—	(2,284)	—	(2,284)
Net loss for the year ended December 31, 2024	—	—	—	—	(147,791)	(147,791)
Balance at December 31, 2024	78,397,380	$ 3	$ 773,565	$ (3,719)	$ (702,022)	$ 67,827

See Notes to Consolidated Financial Statements

MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	For the Years Ended December 31,	
	2024	2023
Cash flows from operating activities:		
Net loss	$ (147,791)	$ (84,027)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share-based compensation expense	25,191	27,716
Foreign currency loss (gain)	2,886	(9,300)
Depreciation and amortization	12,828	13,730
Net change in right-of-use assets and liabilities	16	(222)
Gain on termination of lease liabilities	(172)	—
Loss on disposal of equipment, furniture and fixtures	9	13
Loss on equity method investment	17	6
Amortization of interest on asset retirement obligations	209	177
Amortization of debt discount	1,103	1,083
Fair value adjustment	—	(499)
Impairment of acquired in-process research and development and right-of-use assets	—	1,149
Gain on sale of nonfinancial assets	(28,434)	(54,208)
(Increase) decrease in operating assets:		
Accounts receivable - related party	6,325	9,975
Contract assets - related party	(954)	—
Inventory	(387)	—
Prepaid expenses	(1,328)	2,690
Tax incentive receivable	4,055	(5,148)
Other current assets	(2,302)	222
Other assets, net	759	(1,809)
Increase (decrease) in operating liabilities:		
Accounts payable	10,738	2,330
Accrued expenses	(13,959)	(382)
Other current liabilities	32	(1,355)
Deferred revenue - related party	26,664	(7,506)
Net cash used in operating activities	(104,495)	(105,365)
Cash flows from investing activities:		
Purchase of property, plant and equipment	(4,955)	(20,174)
Proceeds from sale of nonfinancial assets	28,434	54,208
Net cash provided by investing activities	23,479	34,034
Cash flows from financing activities:		
Exercise of share options	—	10
Payments of withholdings on shares withheld for income taxes	(2,340)	(1,519)
Proceeds from the issuance of ordinary shares	59,390	91,950
Issuance costs in connection with ordinary shares	(2,516)	(6,418)
Net cash provided by financing activities	54,534	84,023
Net (decrease) increase in cash, cash equivalents and restricted cash	(26,482)	12,692
Effect of exchange rate changes on cash, cash equivalents and restricted cash	1,501	2,441
Cash, cash equivalents and restricted cash at beginning of the year	130,649	115,516
Cash, cash equivalents and restricted cash at end of the year	$ 105,668	$ 130,649
Supplemental disclosure of non-cash transactions:		
Fixed asset acquisition included in accounts payable and accrued expenses	$ 851	$ 2,607
Change in estimate of asset retirement obligations	$ 345	—
Issuance of shares in connection with asset acquisition	$ —	$ 209
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 12,029	$ 13,054

See 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 genetic medicines company with a broad pipeline of late-stage clinical programs, including Parkinson's disease, radiation-induced xerostomia and AIPL1-associated retinal dystrophy. MeiraGTx clinical programs use targeted local delivery of small doses of genetic medicines to treat both inherited and more common conditions with severe unmet need. The successful development of the clinical pipeline is supported by the Company's internal end-to-end manufacturing capabilities. The Company has two viral vector production facilities for good manufacturing practices ("GMP"), internal plasmid production for GMP, as well as an in-house Quality Control hub for stability and release, all fit for IND through commercial supply. In addition, the Company has developed a proprietary manufacturing platform with leading yield and quality aspects and commercial readiness. The Company's core capabilities in viral vector and capsid optimization allow increased potency, decreased dose and significantly reduced cost of goods for its genetic medicines. The Company has developed a potentially transformative gene regulation platform using bespoke synthetic riboswitch technology invented in-house that allows for the precise, dose-responsive expression of any transgene under the control of oral small molecules. The Company is focusing the riboswitch platform on *in vivo* delivery of biologic therapeutics such as the metabolic peptides GLP-1, GIP, glucagon, amylin, PYY and leptin via oral small molecules, as well as cell therapy for oncology and autoimmune diseases, and long-term intractable pain. The Company has developed unique comprehensive technology capabilities to apply genetic medicine to more common diseases, increasing efficacy, addressing novel targets, and expanding access in some of the largest disease areas where the unmet need remains high.

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 $100.0 million in March 2019 and a $30.0 million milestone payment in December 2021. The Company also received funding for certain research, manufacturing, clinical development and commercialization costs, and had the potential to obtain additional milestone payments upon the achievement of such milestones and royalties on future net sales of products. On December 20, 2023, the Company entered into an Asset Purchase Agreement ("Asset Purchase Agreement") with Janssen pursuant to which the Company sold and assigned to Janssen, and Janssen purchased and assumed, that certain License Agreement, dated February 5, 2019, by and between UCL Business Plc (now UCL Business Ltd.) ("UCLB"), on the one hand, and MeiraGTx UK II Limited and MeiraGTx Limited, on the other hand (the "UCLB RPGR License Agreement"), relating to the research, development, manufacture and exploitation of the RPGR Product, and other related assets as described in the Asset Purchase Agreement. In connection with entering into the Asset Purchase Agreement, the Company entered into a Termination Agreement with Janssen terminating the Collaboration Agreement. The Company and Janssen also entered into a Supply Agreement on December 20, 2023 pursuant to which the Company agreed to manufacture and supply the RPGR Product for Janssen.

Under the Asset Purchase Agreement, Janssen paid the Company a non-refundable upfront cash payment of $65.0 million in December 2023. Additionally, pursuant to and subject to the terms and conditions set forth in the Asset Purchase Agreement, Janssen agreed to pay the Company future contingent consideration of up to an aggregate of $350.0 million, as follows: (i) a milestone payment of $50.0 million in connection with the achievement of the initiation of the extension study for the Phase 3 LUMEOS clinical trial for the RPGR Product; (ii) $10.0 million upon completion of certain specified development services for the drug substance for the RPGR Product; (iii) $5.0 million upon completion of certain specified development services for the drug product for the RPGR Product; (iv) $175.0 million upon the first commercial sale of an RPGR Product in the United States; (v) $75.0 million upon the first commercial sale of an RPGR Product in at least one of the United Kingdom, France, Germany, Spain and Italy;

(vi) $25.0 million upon completion of the transfer of certain manufacturing technology for drug substance and drug product from the Company to Janssen; and (vii) $10.0 million upon regulatory approval of a Janssen-selected manufacturing facility in each of the United States and European Union for commercial manufacture of the RPGR Product. As of December 31, 2024, we have received $60.0 million in milestone payments from Johnson & Johnson Innovative Medicine. Janssen is also responsible for any royalty or milestone amounts that become payable on the RPGR Product under the UCLB RPGR License Agreement.

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 Updates ("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, 2024 totaled $702.0 million, 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; and dependence on key personnel. For the year ended December 31, 2024, the Company used $104.5 million 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, 2024, the Company had cash, cash equivalents and restricted cash in the amount of $105.7 million, which consisted of depository and money market accounts held at large international banks. The Company estimates that its cash and cash equivalents on hand, accounts receivable – related party and tax incentive receivable at December 31, 2024 will be sufficient to cover its expenses for at least the next twelve months from the date of issuance of these consolidated financial statements.

Risks and Uncertainties

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

The Company's capital resources and operations to date have been funded primarily with the proceeds from the Collaboration Agreement, Asset Purchase Agreement and private and public equity offerings, as well as the proceeds from the debt financing described in Note 13. In the future, the Company may seek to raise additional capital through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable it to complete the development and potential commercialization of its product candidates.

2. Summary of Significant Accounting Policies

Consolidation

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

MeiraGTx Limited, a limited company 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");
MeiraGTx Belgium, a private company with limited liability incorporated under the laws of Belgium ("Meira Belgium");
BRI-Alzan, Inc., a Delaware corporation;
MeiraGTx Bio Inc., a Delaware corporation;
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;
MeiraGTx Therapeutics, Inc., a Delaware corporation;
MeiraGTx UK Limited, a limited company incorporated under the laws of England and Wales;
MeiraGTx Neuro I, LLC, a Delaware limited liability company;
MeiraGTx Neuro II, LLC, a Delaware limited liability company;
MeiraGTx Manufacturing Limited, a limited company incorporated under the laws of England and Wales;
MeiraGTx Ocular UK Limited, a limited company incorporated under the laws of England and Wales;
MeiraGTx Gene Regulation Limited, a limited company incorporated under the laws of England and Wales; and
MeiraGTx Neuro UK Limited, a limited company incorporated under the laws of England and Wales.

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

Use of Estimates

Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these consolidated financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. In preparing these consolidated financial statements, management used significant estimates in the following areas, among others: collaboration and service revenue, fair value of nonfinancial assets, stand-alone selling price and material rights in connection with the Asset Purchase and Supply Agreements, the accounting for research and development costs, share-based compensation, leases, asset retirement obligations, fair value of financial instruments and tax incentive receivable.

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 held at large international banks that are readily convertible into cash.

Restricted Cash

Restricted cash represents a guarantee put in place as required by the terms of the research and innovation grant from IDA Ireland which offers financial assistance in establishing the Company's operations in Shannon, Ireland. The following table provides a reconciliation of the components of cash and cash equivalents and restricted cash reported in the Company's consolidated balance sheets to the total of the amount presented in the consolidated statements of cash flows (in thousands):

	December 31, 2024	December 31, 2023
Cash and cash equivalents	$ 103,659	$ 129,566
Restricted cash	2,009	1,083
Total cash, cash equivalents and restricted cash in the condensed consolidated statement of cash flows	$ 105,668	$ 130,649

Inventory

The Company's inventory consists entirely of raw materials and is valued at the lower of cost or net realizable value. The Company regularly reviews its inventory quantities and, when appropriate, records a provision for obsolete and excess inventory to derive the new cost basis. The Company has not recognized a provision for obsolete and excess inventory as of December 31, 2024.

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 United Kingdom ("UK") research and development tax incentive programs under which it is eligible to receive a cash refund from His 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 euros or total aggregate assets less than 86.0 million euros 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, 2024 and 2023, the Company recorded reductions to research and development expenses of $5.5 million and $5.1 million, respectively.

In addition, the Company incurs Value Added Tax ("VAT") on services provided by UK and European Union 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 $2.0 million and $0.6 million as of December 31, 2024 and 2023, respectively, which is included in other current assets in the accompanying consolidated balance sheets.

Fair Value Measurements

Fair value is defined as the price that would be received upon sale of an asset or paid upon transfer of a liability in an orderly transaction between market participants at the measurement date and in the principal or most advantageous market for that asset or liability. The fair value should be calculated based on assumptions that market participants would use in pricing the asset or liability, not on assumptions specific to the entity. In addition, the fair value of liabilities should include consideration of non-performance risk including the Company's own credit risk.

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

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

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

		Fair Value Measurement Using:		
Description	December 31, 2024	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Cash equivalents	$ 80,930	$ 80,930	$ —	$ —
Restricted cash	$ 2,009	$ 2,009	$ —	$ —

		Fair Value Measurement Using:		
Description	December 31, 2023	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Cash equivalents	$ 46,868	$ 46,868	$ —	$ —
Restricted cash	$ 1,083	$ 1,083	$ —	$ —

At December 31, 2024, the Company believes the carrying value of the Tranche 1 Notes (as defined in Note 13) approximates fair value as the interest rate is reflective of the rate the Company could obtain on debt with similar terms and conditions.

Equity Method and Other Investments

The Company accounts for equity investments under the equity method of accounting when the requirements for consolidation are not met, and the Company has significant influence over the operations of the investee. Equity method investments are initially recorded at cost and subsequently adjusted for the Company's share of net income or loss and cash contributions and distributions and are included in equity method and other investments in the accompanying consolidated balance sheets. Equity investments that do not result in consolidation and are not accounted for under the equity method are measured at fair value, with any changes in fair value recognized in net income (loss). For any such investments that do not have readily determinable fair values, the Company elects the measurement alternative to measure the investments at cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer. Equity method investments are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. If it is determined that a loss in value of the equity method investment is other than temporary, an impairment loss is measured based on the excess of the carrying amount of an investment over its estimated fair value. Impairment analyses are based on current plans, intended holding periods, and available information at the time the analysis is prepared.

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 limits. 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 use in the Company's operations. The licensed technology is being amortized on a straight-line basis over 7 years, which represents the estimated period 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 terms of the leases (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
Furniture and fixtures	5 years
Manufacturing equipment	7 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 did not record any material impairment charges in 2024 or 2023.

Leases

The Company accounts for leases in accordance with FASB Topic ASC 842, *Leases* ("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 – operating leases, net and lease obligations 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 – finance leases, net 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 lease terms 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. 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 (in thousands):

	For the Years Ended December 31,	
	2024	2023
Balance at beginning of period	$ 2,401	$ 2,179
Change in estimate	345	—
Assignment of leases to Johnson & Johnson Innovative Medicine	(115)	—
Amortization of interest	209	177
Effects of exchange rate changes	(19)	45
Balance at end of period	$ 2,821	$ 2,401

IDA Ireland Grant

In August 2021, Meira Ireland entered into an agreement pursuant to which it received a grant from IDA Ireland for financial assistance in establishing its operations in Shannon, Ireland. Under the terms of the grant, Meira Ireland is eligible to receive the lesser of €1.0 million or €10,000 for each job created (the "employment grant") and the lesser of €1.2 million or 4% of the actual expenditure on the provision of machinery and equipment (the "capital grant"). Meira Ireland may apply for a drawdown of the employment grant once a job has been created and the position has been held for a period of at least one month, and may apply for a drawdown of the capital grant once an eligible asset has been purchased and installed, conditioned on the creation of a cumulative number of jobs by the end of the immediately preceding year. An aggregate of 100 jobs must be created to receive the maximum benefit under the capital grant. An application for a drawdown must be accompanied by an audit certification for compliance with the terms of the grant. The Company has a guarantee in place with a bank in favor of IDA Ireland, pursuant to which it restricts cash in the amount of claims made under the grant such that the Company maintains the funds to cover any portion of the grant income that may become repayable in the future. This amount is presented as restricted cash in the accompanying consolidated balance sheet. All grant drawdowns were required to be completed by December 31, 2024, and the agreement terminates on the later of five years from the date of the last payment from the grant or five

years from completion of the capital investment, which is expenditure of at least €30.0 million on eligible machinery and equipment.

The Company recognizes grant income when there is reasonable assurance that the Company will comply with the conditions attached to the grant and that it will receive the grant. Grant income from the employment grant is recognized as a deduction from the amount of the related expense, and grant income from the capital grant is deducted from the carrying amount of the related asset and recognized in income over the asset's useful life in the form of a reduced depreciation charge. The Company received its first drawdown under the grant in 2023, which was comprised of $0.6 million for the employment grant and $0.4 million for the capital grant. The Company received its second drawdown under the grant in 2024, which was comprised of $0.5 million for the employment grant and $0.5 million for the capital grant. During the years ended December 31, 2024 and 2023, respectively, the Company recognized $0.6 and $1.0 million of grant income as a reduction of research and development expenses in the accompanying consolidated statements of operations and comprehensive loss.

During the five-year period ending on the termination of the grant agreement, Meira Ireland must maintain compliance with the terms of the grant. If the total number of jobs is less than 100 at the time of IDA Ireland's annual review, the Company may have to repay a portion of the capital grant, and if a job for which the Company received employment grant funding remains vacant for a period in excess of six calendar months, the Company may have to repay the employment grant received for that job.

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. The Company accounts for forfeitures of stock option awards as they occur. 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.

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 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.*

Expected volatility is based on an analysis of guideline companies and the Company's own volatility 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 Share Units

The Company grants restricted share units ("RSUs") to employees, non-employee members of the Company's board of directors and non-employee consultants as compensation for services performed. Awards of RSUs are accounted for in accordance with ASC 718. ASC 718 requires all share-based payments to employees, non-employee members of the Company's board of directors and non-employee consultants, 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.

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 Company concludes that some or all aspects of the arrangement are within the scope of ASC 808 and do not represent a transaction with a customer, the Company recognizes its allocation of the shared costs incurred with respect to the jointly conducted activities pursuant to ASC 730, *Research and Development* ("ASC 730"). If the Company concludes that some or all aspects of the arrangement represent a transaction with a customer, the Company accounts for those aspects of the arrangement within the scope of ASC 606. 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

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.

At inception, the Company determines whether contracts are within the scope of ASC 606 or other topics. For contracts that are determined to be within the scope of 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 the Company 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, 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.

If there are multiple performance obligations, the Company allocates the transaction price to each performance obligation based on their estimated standalone selling prices ("SSP"). The Company estimates the SSP for each

performance obligation by considering information such as market conditions, entity-specific factors, and information about its customer that is reasonably available. The Company considers estimation approaches that allow it to maximize the use of observable inputs. These estimation approaches may include the adjusted market assessment approach, the expected cost plus a margin approach or the residual approach. The Company also considers whether to use a different estimation approach or a combination of approaches to estimate the SSP for each performance obligation. Developing certain assumptions (e.g., treatable patient population, expected market share, probability of success and product profitability, and discount rate based on weighted-average cost of capital) to estimate the SSP of a performance obligation requires significant judgment.

The Company records amounts as contract assets when the right to consideration is deemed unconditional. Contract assets are reclassified as accounts receivable once billed. 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 and 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: Under the Collaboration Agreement, the Company incurred research and development costs, with Johnson & Johnson Innovative Medicine responsible for up to 100% of the costs, depending on the type of research and development services being performed. The Company recorded costs associated with the development activities as research and development expenses in the consolidated statements of

operations and comprehensive loss consistent with ASC 730. The reimbursement of the research and development costs by Johnson & Johnson Innovative Medicine was representative of the joint risk sharing nature of the arrangement. The Company considered the guidance in ASC 808 and recognizes the payments received from Johnson & Johnson Innovative Medicine as a reduction to research and development expense when the related costs are incurred. Under the Asset Purchase Agreement, research and development services (PPQ services) are recorded as incurred under cost of service revenue – related party.

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the customer's discretion are generally considered options. The Company assesses if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations at the outset of the arrangement.

Customer Options: Customer options are evaluated at contract inception to determine whether those options provide a material right (i.e., an optional good or service offered for free or at a discount) to the customer. If the customer options represent a material right, the material right is treated as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the standalone selling price. As a practical alternative to estimating the standalone selling price of a material right when the underlying goods or services are both (i) similar to the original goods or services in the contract and (ii) provided in accordance with the terms of the original contract, the Company allocates the total amount of consideration expected to be received from the customer to the total goods or services expected to be provided to the customer. Amounts allocated to any material right are recognized as revenue when or as the related future goods or services are transferred or when the option expires.

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 our subsidiaries 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 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, 2024 and 2023, the Company recorded unrecognized tax positions of $2.2 million and $2.0 million, 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 assumed to be outstanding during the period of computation. Diluted net loss per ordinary share is computed similar to basic net loss per share except that the denominator is increased to include the number of additional ordinary shares that would have been outstanding if the potential ordinary 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, 2024	December 31, 2023
Share options	8,232,587	8,226,707
Restricted share units	4,252,250	2,661,250
Deferred share units	—	185,000
Warrants	700,000	700,000
	13,184,837	11,772,957

Other Comprehensive Income (Loss)

Other comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. The only component of other comprehensive income (loss) impacting the Company is foreign currency translation.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to

allocate resources in assessing performance. The Company has one reportable and operating segment, which is the development and manufacturing of genetic medicines, for purposes of reporting financial condition and results of operations. The Company's chief operating decision maker ("CODM") is the chief executive officer.

The accounting policies of its segment are the same as those described in the summary of significant accounting policies. The CODM allocates resources and assesses performance of the Company's single reportable segment by regularly reviewing the segment net loss that also is reported on the consolidated statement of operations and comprehensive loss as net loss.

The following table sets forth information about the Company's single reportable segment and the significant expenses reviewed by the CODM, including a reconciliation to net loss (in thousands):

	For the Years Ended December 31,	
	2024	2023
Service revenue - related party	$ 33,279	$ —
License revenue - related party	—	14,017
Operating expenses:		
Cost of service revenue - related party	23,791	—
General and administrative	39,389	31,522
Clinical programs:		
Botaretigene sparoparvovec	1,250	55,518
AAV-hAQP1	17,307	15,772
AAV-CNGB3 / AAV-CNGA3	(969)	2,184
AAV-GAD	6,411	7,598
Other ocular diseases	1,763	—
Manufacturing	53,445	50,221
Preclinical programs:		
Gene regulation	10,509	8,324
Neurodegenerative diseases	1,608	2,242
Preclinical ocular diseases	2,474	2,849
Other research and development[1]	2,494	3,831
Johnson & Johnson Innovative Medicine reimbursement	—	(70,429)
Share-based compensation	25,191	27,716
Depreciation and amortization	12,828	13,730
Total operating expenses	197,491	151,078
Other segment items[2]	16,421	53,034
Segment net loss	$ (147,791)	(84,027)
Adjustments or reconciling items	—	—
Net loss	$ (147,791)	$ (84,027)

[1] Other research and development is comprised of all other costs including payroll and payroll related costs, travel, rent and facilities costs and other non-program specific expenses.

[2] Other segment items is comprised of foreign currency (loss) gain, interest income, interest expense, gain on sale of nonfinancial assets and fair value adjustment.

The Company's service and license revenue, research funding and deferred revenue from the Collaboration Agreement and the Asset Purchase Agreement and related agreements were generated in the United Kingdom.

The following table summarizes long-lived assets by geographical area (in thousands):

	December 31, 2024	December 31, 2023
United States	$ 7,209	$ 11,071
United Kingdom	28,419	33,798
European Union	100,845	112,487
	$ 136,473	$ 157,356

Recent Accounting Pronouncements Adopted

In November 2023, the FASB issued ASU 2023-07, *Segment Reporting - Improvements to Reportable Segment Disclosures*, which updates reportable segment disclosure requirements, primarily through enhanced disclosures about significant segment expenses and information used to assess segment performance. The Company adopted this standard on January 1, 2024 for the 2024 fiscal year, and for interim periods beginning January 1, 2025. The adoption of this standard did not have a material impact on the Company's consolidated financial statements. Refer to Segment Information within this footnote for additional information.

Recent Accounting Pronouncements Not Yet Adopted

In October 2023, the FASB issued ASU 2023-06, *Disclosure Improvements: Codification Amendments in Response to the SEC's Disclosure Update and Simplification Initiative*. This update includes a number of amendments to clarify or improve disclosure and presentation requirements of a variety of topics in order to allow users to more easily compare entities subject to the SEC's existing disclosures with those entities that were not previously subject to the requirements and to align the requirements in the FASB accounting standard codification with the SEC's regulations. The effective date for each amendment will be the date on which the SEC's removal of that related disclosure requirement from Regulation S-X or Regulation S-K becomes effective, with early adoption prohibited. The Company is currently evaluating the impact of these amendments.

In December 2023, the FASB issued ASU 2023-09, *Improvements to Income Tax Disclosures*, which requires that an entity disclose specific categories in the effective tax rate reconciliation as well as provide additional information for reconciling items that meet a quantitative threshold. Further, the ASU requires certain disclosures of state versus federal income tax expense and taxes paid. This ASU is effective for fiscal years beginning after December 15, 2024. The Company does not expect the adoption of this ASU to have a material impact on its consolidated financial statements.

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement: Reporting Comprehensive Income: Expense Disaggregation Disclosures (Subtopic 220-40)*, which requires public business entities to disclose additional information about specific expense categories in the notes to financial statements at interim and annual reporting periods. In January 2025, the FASB issued ASU No. 2025-01, *Clarifying the Effective Date*, which revised the effective date of ASU No. 2024-03 for interim periods. The guidance is effective for annual periods beginning after December 15, 2026, and interim periods within fiscal years beginning after December 15, 2027. The Company is currently assessing the impact of ASU 2024-03 and ASU 2025-01 on its consolidated financial statements.

3. Equity Method and Other Investments

The Company's investments consist of the following (in thousands):

		December 31, 2024		
Investee	Investment Type	Ownership Percentage	Carrying Value	Cost Basis
Visiogene LLC	Equity Method Investment	25 %	$ 5,133	$ 5,165
Other	Equity Investment	0.9 %	1,616	1,500
Total equity method and other investments			$ 6,749	$ 6,665

Visiogene LLC

On January 4, 2021, the Company and Visiogene LLC ("Visiogene") entered into a License and Investment Agreement ("Visiogene License Agreement") for an exclusive, worldwide license to certain of Visiogene's intellectual property relating to ocular gene therapy. Concurrently, the Company and Visiogene entered into a Preferred Unit Purchase Agreement ("Visiogene Unit Agreement") pursuant to which the Company purchased 3,000,000 Visiogene preferred units. In connection with the two Visiogene agreements, the Company paid $5.0 million in cash and issued to Visiogene 75,000 ordinary shares of the Company with a fair market value of $1.2 million based on the closing price of the Company's ordinary shares on the date of closing.

The Company accounted for the payments under the Visiogene License Agreement and Visiogene Unit Agreement as a basket transaction and allocated $1.0 million to the Visiogene License Agreement and the remaining $5.2 million was allocated to the Visiogene preferred units. The $1.0 million allocated to the Visiogene License Agreement was expensed as acquired in-process research and development as the Company determined there was no alternative future use. The Company accounts for this investment using the equity method of accounting.

During the years ended December 31, 2024 and 2023, the Company recorded de minimis research and development expenses related to the Company's share of Visiogene's losses.

4. Prepaid Expenses

Prepaid expenses at December 31, 2024 and 2023 consist of the following (in thousands):

	December 31, 2024	December 31, 2023
Manufacturing costs	$ 1,826	38
Clinical trial costs	1,823	$ 1,530
Dues and license fees	1,253	1,439
Insurance	840	861
Facilities costs	657	630
Other	429	199
Research and development	—	685
Consulting	—	243
	$ 6,828	$ 5,625

5. Property, Plant and Equipment, net

Property, plant and equipment, net at December 31, 2024 and 2023 consist of the following (in thousands):

	December 31, 2024	December 31, 2023
Leasehold improvements	$ 99,371	$ 103,082
Manufacturing equipment	23,019	22,646
Laboratory equipment	14,741	15,389
Computer and office equipment	7,292	7,370
Furniture and fixtures	758	734
	145,181	149,221
Less: Accumulated depreciation and amortization	(42,303)	(33,325)
	$ 102,878	$ 115,896

In connection with certain operating leases, the Company has determined that it has asset retirement obligations in the aggregate amount of $5.4 million at the end of those leases. The Company discounted the initial asset retirement obligations using an 8% discount rate and during the year ended December 31, 2024, the Company recorded a change in estimate in connection with five leases using a 15% discount rate. The Company recorded an asset retirement obligation in the aggregate amount of $2.1 million, which is included in leasehold improvements and is being amortized over the term of the respective leases.

Depreciation and amortization expense related to property, plant and equipment was $11.4 million and $12.3 million for the years ended December 31, 2024 and 2023, 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, 2024 and 2023 (in thousands):

	December 31, 2024	December 31, 2023
Licensed Technology	$ 1,971	$ 2,000
Less: Accumulated amortization	(1,150)	(882)
	$ 821	$ 1,118

The intangible asset is being amortized over a period of seven years. Amortization expense of $0.3 million was recorded as a component of research and development expenses for each of the years ended December 31, 2024 and 2023, respectively.

As of December 31, 2024, the expected amortization expense for the next three years is as follows (in thousands):

	Amortization Expense
2025	$ 281
2026	281
2027	259
Total amortization	$ 821

7. Accrued Expenses

Accrued expenses at December 31, 2024 and 2023 were comprised of the following (in thousands):

	December 31, 2024	December 31, 2023
Professional fees	$ 6,326	$ 6,499
Compensation and benefits	11,197	12,129
Clinical trial costs	3,864	8,713
Research and development	2,234	5,834
Manufacturing costs	1,540	2,634
Consulting	1,530	2,104
Fixed assets	326	1,472
Rent and facilities costs	257	142
Interest on Tranche 1 Notes	—	2,936
Other	140	176
	$ 27,414	$ 42,639

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, non-employee members of the Company's board of directors 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 13,654,788 as of December 31, 2024. As of December 31, 2024, 300,888 shares remain available for future issuance. In January 2025, the number of shares available for issuance under the 2018 Incentive Award Plan increased by 3,135,895 shares.

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, 2024 is as follows (in thousands, except share and per share amounts):

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)
Outstanding at December 31, 2023	8,226,707	$ 12.96	6.35 years
Granted	365,100	$ 6.16	
Forfeited	(359,220)	$ 15.32	
Outstanding at December 31, 2024	8,232,587	$ 12.57	5.35 years
Options exercisable at December 31, 2024	6,874,024	$ 13.03	4.83 years
Options vested and expected to vest at December 31, 2024	8,232,587	$ 12.57	5.35 years
Aggregate intrinsic value of options outstanding as of December 31, 2024	$ 1,422		
Aggregate intrinsic value of options exercisable as of December 31, 2024	$ 1,422		

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 Company recorded the following share-based compensation expense in connection with the options for the years ended December 31, 2024 and 2023 (in thousands):

	Years Ended December 31,	
	2024	2023
Research and development	$ 6,062	$ 8,577
General and administrative	3,892	5,054
Total share-based compensation	$ 9,954	$ 13,631

The total fair value of options vested during the years ended December 31, 2024 and 2023 was $12.1 million and $15.3 million, respectively.

The weighted average grant date fair value of options granted during the years ended December 31, 2024 and 2023 was $3.91 per share and $5.67 per share, 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):

	2024	2023
Risk-free interest rate	4.04 - 4.17%	3.86 - 4.48%
Expected volatility	67%	72%
Expected dividend yield	0%	0%
Expected term (in years)	3.6 - 6.1	3.6 - 6.1

As of December 31, 2024, the total compensation expense relating to unvested options granted that had not yet been recognized was $8.5 million, which is expected to be recognized over a period of 3.2 years. The Company will issue shares upon exercise of options from ordinary shares reserved under the Plans.

Restricted Share Units

A summary of the Company's RSU activity related to employees, non-employee members of the board of directors and non-employee consultants for the year ended December 31, 2024 is as follows:

	Number of Restricted Share Units	Weighted-Average Grant Date Fair Value
Outstanding at December 31, 2023	2,661,250	$ 15.24
Granted	2,638,500	$ 5.97
Vested	(1,002,500)	$ 18.14
Forfeited	(45,000)	$ 4.87
Outstanding at December 31, 2024	4,252,250	$ 8.91

RSUs granted generally vest 50% on the second anniversary of the date of grant and 25% on the third and fourth anniversaries of the date of grant. Annual RSUs granted to directors generally vest in a single installment on the earliest to occur of the first anniversary of the grant date or the day immediately prior to the date of the next annual meeting of the Company's shareholders occurring after the date of grant. The RSUs granted to the directors in June 2021 will be paid on or within 30 days after the date a director ceases to serve on the board. For RSUs granted in future years, the directors may elect whether to defer the payment of their annual RSU awards under the Deferred Compensation Plan for Non-Employee Directors, which was adopted by the board on December 17, 2021. As of December 31, 2024, there were 272,500 vested shares that have been deferred. 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, as applicable, in the consolidated statements of operations and comprehensive loss.

The company recorded the following share-based compensation expense in connection with the RSUs for the years ended December 31, 2024 and 2023 (in thousands):

	Years Ended December 31,	
	2024	2023
Research and development	$ 5,070	$ 4,203
General and administrative	10,167	9,882
Total share-based compensation	$ 15,237	$ 14,085

As of December 31, 2024, the total compensation expense relating to unvested RSUs granted that had not yet been recognized was $21.9 million, which is expected to be recognized over a period of 3.3 years.

To satisfy employee minimum statutory tax withholding requirements for restricted share units that vest, the Company withholds a portion of the vesting ordinary shares. During the years ended December 31, 2024 and 2023, the Company withheld 377,152 and 237,859 ordinary shares with a total value of approximately $2.3 million and $1.5 million, respectively. These amounts are presented as a cash outflow from financing activities in the accompanying consolidated statement of cash flows.

During the years ended December 31, 2024 and 2023 the Company recognized total share-based compensation expense in the accompanying consolidated statements of operations and comprehensive loss as follows (in thousands):

	Years Ended December 31,	
	2024	2023
Research and development	$ 11,132	$ 12,780
General and administrative	14,059	14,936
Total share-based compensation	$ 25,191	$ 27,716

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, 2024 and 2023.

9. Ordinary Shares

2024

At-the-Market

In December 2023, the Company entered into an “at-the-market” sales agreement with BofA Securities, Inc., or BofA, pursuant to which the Company may sell from time to time, ordinary shares having an aggregate offering price of up to $100.0 million through BofA, acting as the Company’s agent. During the year ended December 31, 2024, the Company raised gross proceeds of $8.4 million through the sale of 1,508,517 ordinary shares pursuant to an “at-the-market” equity offering program. Under the “at-the-market” equity program which is currently effective and may remain available for the Company to use in the future, the Company may sell an additional $91.6 million of ordinary shares. Whether the Company chooses to affect future sales under the “at-the-market” equity offering program will depend on a number of factors, including, among others, market conditions and the trading price of the Company’s ordinary shares relative to other sources of capital.

Equity Financing

On August 12, 2024, the Company entered into an underwriting agreement with BofA in connection with the issuance and sale by the Company in a public offering of 12,500,000 of the Company’s ordinary shares at a public offering price of $4.00 per share, less underwriting discounts and commissions, pursuant to an effective shelf registration statement on Form S-3 (Registration No. 333-276183) and a related prospectus supplement filed with the SEC. The closing of the offering occurred on August 13, 2024. The Company received gross proceeds from the offering of $50.0 million and incurred underwriting discounts and commissions and estimated offering expenses of approximately $1.9 million.

On August 12, 2024, the Company agreed to sell shares to an accredited investor (the "Investor") through a private placement rather than through the public offering and as a result, on August 23, 2024, the Company entered into a securities purchase agreement with the Investor, pursuant to which the Company, in a private placement, agreed to issue and sell to the Investor 250,000 ordinary shares at a purchase price of $4.00 per share, for gross proceeds of $1.0 million (the "Private Placement"). The closing of the Private Placement occurred on August 29, 2024.

2023

May 2023 Private Placement

On May 3, 2023, the Company entered into a securities purchase agreement with certain accredited investors, pursuant to which the Company, in a private placement, agreed to issue and sell an aggregate of 10,773,913 ordinary shares at a purchase price of $5.75 per share, for gross proceeds of approximately $62.0 million and incurred issuance costs of approximately $4.1 million. The closing occurred on May 5, 2023.

Sanofi Private Placement

On October 30, 2023, the Company entered into an Investment Agreement with Sanofi Foreign Participations B.V., a wholly-owned subsidiary of Sanofi, and solely for the limited purposes set forth therein, Sanofi, pursuant to which, the Company, in a private placement, issued an aggregate of 4,000,000 ordinary shares, at a purchase price of $7.50 per share for gross proceeds of $30.0 million and incurred issuance costs of approximately $2.3 million.

10. Income Taxes

For the years ended December 31, 2024 and 2023, the Company recognized a tax benefit of $0.

As of December 31, 2024, 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 (in thousands):

	Federal	State/City
United Kingdom	$ 203,678	$ —
United States	$ 74,348	$ 19,285
Ireland	$ 78,309	$ —
Other	$ 29,987	$ —

All of the Company's carryforward tax losses will be indefinitely carried forward, with the exception of federal U.S. NOLs in the amount of $0.2 million as of December 31, 2024, which will begin to expire in 2037 and state NOLs in the amount of $19.0 million as of December 31, 2024, which will begin to expire in 2036. Also, as of December 31, 2024, the Company had orphan drug and research and development credits in the U.S. in the amount of $22.5 million which will begin to expire in 2035 and research and development credits of $1.9 million in the UK which can be carried forward indefinitely. 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 of the Internal Revenue Code, as well as 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 August 2024, 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, but there was not a limit for utilizing these losses.

The Company's pre-tax income (loss) is as follows (in thousands):

	December 31, 2024	December 31, 2023
United Kingdom	$ (62,760)	$ 12,881
United States	(57,580)	(63,017)
Ireland	(25,762)	(29,965)
Other	(1,689)	(3,926)
	$ (147,791)	$ (84,027)

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 (in thousands):

	December 31, 2024		December 31, 2023	
Statutory rate	(36,948)	25.00 %	(19,746)	23.50 %
Permanent differences - other	4,264	(2.88)%	2,391	(2.85)%
RTP and other adjustment	4,252	(2.88)%	(1,165)	1.39 %
State and local rate, net of federal tax	(634)	0.43 %	(698)	0.83 %
U.K. tax credit	6,476	(4.38)%	(4,028)	4.79 %
U.S. tax credit	(3,352)	2.27 %	(9,830)	11.70 %
Foreign tax rate differential	4,751	(3.21)%	4,558	(5.42)%
UK rate change	—	— %	239	(0.28)%
US state rate change	(309)	0.21 %	15,394	(18.32)%
Section 162(m) deferred adjustment	1,568	(1.06)%	2,728	(3.25)%
Disallowed interest	(4,106)	2.76 %	2,812	(3.35)%
Change in valuation allowance	24,038	(16.26)%	7,345	(8.74)%
Actual income tax benefit effective tax rate	—	— %	—	— %

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

	December 31, 2024	December 31, 2023
Current Tax Expense/(Benefit)		
United Kingdom	—	—
United States	—	—
Other	—	—
Total Current	—	—
Deferred Tax Expense/(Benefit)		
United Kingdom	(9,344)	2,393
United States	(11,405)	(6,251)
Ireland	(3,134)	(3,963)
Netherlands	(155)	(1,840)
Total Deferred	(24,038)	(9,661)
Change in Valuation Allowance	24,038	9,661
Total Income Tax Expense/(Benefit)	—	—

Deferred Tax Assets/(Liabilities) (in thousands):

	December 31, 2024	December 31, 2023
Deferred Tax Assets:		
Net operating loss carryforwards	$ 85,308	$ 70,650
Interest expense	6,736	—
Capitalized research and development	26,312	19,606
Share-based compensation	11,921	14,290
R&D credit	22,160	21,687
Lease liability	2,767	4,070
Deferred tax assets	155,204	130,303
Less: valuation allowance	(149,382)	(125,884)
Deferred Tax Liabilities:		
Depreciation	(2,192)	(1,763)
Right of use assets	(2,099)	(3,777)
Other	(1,531)	1,121
Net deferred tax liability	$ —	$ —

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, 2024 and 2023 because the Company's management has determined that it is more likely than not that these assets will not be fully realized.

As of December 31, 2024 and 2023, the Company recorded unrecognized tax positions of $2.2 million and $2.0 million, respectively. The unrecognized tax positions are netted with deferred tax assets above with a full valuation allowance. The changes to unrecognized tax positions for 2024 and 2023 were as follows (in thousands):

	December 31, 2024	December 31, 2023
Unrecognized tax benefits as of January 1	$ 2,029	$ 937
Gross increases/(decreases) related to current year	505	756
Gross increases/(decreases) related to prior years	(285)	336
Unrecognized tax positions as of December 31	$ 2,249	$ 2,029

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2024 and 2023, 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, various foreign jurisdictions and various U.S. state jurisdictions. In the U.S., all years remain subject to examination. The earliest year subject to examination in the UK is 2023.

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

11. Related Party Transactions

Relationship with Johnson & Johnson Innovative Medicine

Collaboration Agreement

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

Pursuant to the Collaboration Agreement, the Company and Johnson & Johnson Innovative Medicine also agreed on a research collaboration to develop a pipeline of preclinical inherited retinal disease gene therapy candidates ("Research IRD Product Candidates"). The parties agreed to select and prioritize the Research IRD Product Candidates and Johnson & Johnson Innovative Medicine had 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 was to continue in effect, on a product-by-product and country-by-country basis, until such time as the royalty terms expired in such country. The Company had determined enforceable rights existed in the Collaboration Agreement as the termination clauses were substantive termination penalties by way of the non-refundable upfront fee and the reversion of any licensed intellectual property granted to Johnson & Johnson Innovative Medicine upon the termination of the agreement.

Under the Collaboration Agreement, the Company and Johnson & Johnson Innovative Medicine were jointly developing Clinical IRD Product Candidates to permit Johnson & Johnson Innovative Medicine to commercialize such Clinical IRD Product Candidates under an exclusive license from the Company. In general, the Company had 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 agreed to manufacture these products in its GMP manufacturing facilities for both clinical and commercial supply. Johnson & Johnson Innovative Medicine agreed to pay 100% of the clinical and commercialization costs of the products and the Company was eligible to receive untiered 20% royalties on net sales of products and additional development and commercialization milestones up to $340.0 million. The Company received a milestone payment of $30.0 million in December 2021. In connection with entering into the Asset Purchase Agreement, the Company entered into a Termination Agreement with Johnson & Johnson Innovative Medicine terminating the Collaboration Agreement.

Asset Purchase and Related Agreements

On December 20, 2023, the Company entered into the Asset Purchase Agreement with Johnson & Johnson Innovative Medicine pursuant to which the Company sold and assigned to Johnson & Johnson Innovative Medicine, and Johnson & Johnson Innovative Medicine purchased and assumed, the UCLB RPGR License Agreement relating to the research, development, manufacture and exploitation of the RPGR Product, and other related assets as described in the Asset Purchase Agreement. Simultaneously, the Company and Johnson & Johnson Innovative Medicine also entered into a Supply Agreement pursuant to which the Company agreed to manufacture and supply the RPGR Product for Johnson & Johnson Innovative Medicine. Under the Supply Agreement, MeiraGTx UK II, together with its affiliates, will manufacture commercial supply of the RPGR Product for Johnson & Johnson Innovative Medicine for an initial term of four years, with Johnson & Johnson Innovative Medicine having an

option to extend the Supply Agreement for a fifth year upon written notification. Johnson & Johnson Innovative Medicine may terminate the Supply Agreement for convenience upon 90 days' written notice with payment of a termination fee. Under the Asset Purchase Agreement, Johnson & Johnson Innovative Medicine paid the Company a non-refundable upfront fee of $65.0 million in December 2023 and the Company is eligible to receive fees from commercial supply of the RPGR Product and in addition, milestones of up to $350.0 million, as follows: (i) a milestone payment of $50.0 million in connection with the achievement of the initiation of the extension study for the Phase 3 LUMEOS clinical trial for the RPGR Product; (ii) $10.0 million upon completion of certain specified development services for the drug substance for the RPGR Product; (iii) $5.0 million upon completion of certain specified development services for the drug product for the RPGR Product; (iv) $175.0 million upon the first commercial sale of an RPGR Product in the United States; (v) $75.0 million upon the first commercial sale of an RPGR Product in at least one of the United Kingdom, France, Germany, Spain and Italy; (vi) $25.0 million upon completion of the transfer of certain manufacturing technology for drug substance and drug product from the Company to Johnson & Johnson Innovative Medicine; and (vii) $10.0 million upon regulatory approval of a Johnson & Johnson Innovative Medicine-selected manufacturing facility in each of the United States and European Union for commercial manufacture of the RPGR Product. As of December 31, 2024, we have received $60.0 million in milestone payments from Johnson & Johnson Innovative Medicine. Johnson & Johnson Innovative Medicine is also responsible for any royalty or milestone amounts that become payable on the RPGR Product under the UCLB RPGR License Agreement.

Revenue Recognition under the Johnson & Johnson Innovative Medicine Agreements

Collaboration Agreement

The Company evaluated the potential performance obligations in the Collaboration Agreement pursuant to ASC 606, 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 were excluded from the initial allocation of transaction price and the Company would have accounted for these options as separate contracts when and if Johnson & Johnson Innovative Medicine had elected 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 included in the transaction price was updated at each reporting date as a change in estimate. The amount related to the unsatisfied portion was recognized as that portion was 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 Johnson & Johnson Innovative Medicine on a product candidate basis. Johnson & Johnson

Innovative Medicine's right to purchase exclusive options to obtain certain development, manufacturing and commercialization rights were accounted for separately as they did not represent material rights, based on the criteria of ASC 606. Upon the exercise of any purchased option by Johnson & Johnson Innovative Medicine, the contract promises associated with an Option Target have used a separate cost-to-cost model for purposes of revenue recognition under ASC 606.

In 2019, the Company received a $100.0 million non-refundable upfront fee from Johnson & Johnson Innovative Medicine and during the year ended December 31, 2021, the Company received a $30.0 million milestone payment. The Company allocated these amounts 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.

Asset Purchase and Related Agreements

The agreements entered into in December 2023 were executed at the same time and were negotiated with a single commercial objective; therefore, the contracts were combined and accounted for as a single contract. These agreements were accounted for as a termination of the existing Collaboration Agreement and the creation of a new contract where the transaction price includes the remaining deferred revenue – related party from the terminated agreement of $30.6 million, the fixed upfront payment of $65.0 million under the Asset Purchase Agreement, and an aggregate of $1.8 million estimated variable consideration for transition services, offset by a credit of $5.1 million for pre-funded inventory, totaling $92.3 million. The transaction price was allocated to four performance obligations on a relative SSP basis, subject to certain exceptions for discounts and variable consideration. As the SSPs are not directly observable for any of the distinct goods and services, the SSPs were estimated based on a valuation. The total transaction price of $92.3 million was allocated to the performance obligations with respect to SSPs as follows: process performance qualification ("PPQ") services in the amount of $2.9 million, net of future billings, material rights representing the commercial supply of RPGR Product and an in-substance contract renewal option in the amount of $6.9 million, manufacturing technology transfer in the amount of $28.7 million, and the sale of nonfinancial assets representing the sale and transfer of all the Company's right, title, and interest in the intellectual property related to the RPGR Product and the assignment of the UCLB RPGR License Agreement to Johnson & Johnson Innovative Medicine in the amount of $53.8 million.

During the year ended December 31, 2024, the Company received a $50.0 million milestone payment in connection with the achievement of the initiation of the extension study for the Phase 3 LUMEOS clinical trial for the RPGR Product. The milestone payment was allocated to the four performance obligations on the same basis noted above increasing the value of each performance obligation as follows: PPQ services in the amount of $1.6 million, material rights representing the commercial supply of RPGR Product and an in-substance contract renewal option in the amount of $3.8 million, manufacturing technology transfer in the amount of $15.6 million, and the sale of nonfinancial assets representing the sale and transfer of all the Company's right, title, and interest in the intellectual property related to the RPGR Product and the assignment of the UCLB RPGR License Agreement to Johnson & Johnson Innovative Medicine in the amount of $29.0 million. Additionally, the Company received a $10.0 million milestone payment in connection with the completion of certain specified development services for the drug substance for the RPGR Product which was allocated to the PPQ services performance obligation. The Company also entered into additional agreements to provide additional services under the Asset Purchase Agreement and related agreements amounting to an aggregate of $5.7 million which was included in the transaction price and allocated to each of the respective performance obligations. Furthermore, the Company recorded certain changes in estimates related to the valuation of its performance obligations.

The transaction price allocated to PPQ services will be recognized over time using an inputs method measure of progress. The transaction price allocated to the material right for the commercial supply of RPGR Product will be

recorded as deferred revenue until Johnson & Johnson Innovative Medicine exercises its option to purchase supply and the Company transfers control of such supply to Johnson & Johnson Innovative Medicine. The transaction price allocated to the in-substance renewal option (material right) will be recorded as deferred revenue until Johnson & Johnson Innovative Medicine exercises the option and the Company transfers control of the underlying goods or services to Johnson & Johnson Innovative Medicine. The Company will account for the exercise of the in-substance renewal option (material right) as a continuation of the existing contract (i.e., a change in the transaction price). The transaction price allocated to the technology transfer will be recognized over time using an inputs method measure of progress. The Company will recognize a gain for the difference between the carrying amount of the nonfinancial assets and the consideration allocated to that unit of account when control of the nonfinancial assets transfers in accordance with ASC 610-20, *Other Income - Gains and Losses from the Derecognition of Nonfinancial Assets*.

During the years ended December 31, 2024 and 2023, the Company recognized a gain of $28.4 and $54.2 million, respectively, related to the sale of nonfinancial assets which is included in other income in the consolidated statement of operations and comprehensive loss.

As of December 31, 2024, the aggregate transaction price allocated to unsatisfied performance obligations was $62.4 million which the Company expects to recognize over an estimated period of approximately 3.0 years.

A summary of the deferred revenue recognition is as follows (in thousands):

Deferred revenue at December 31, 2023	$	36,943
Milestone payment allocated to performance obligations		33,066
Other amounts collected or invoiced		7,809
Deferred revenue recognized as service revenue during the year ended December 31, 2024		(14,035)
Effects of exchange rate changes		(1,380)
Deferred revenue at December 31, 2024	$	62,403

During the year ended December 31, 2024, the Company recognized $14.0 million of deferred revenue – related party as service revenue in connection with PPQ services under the Asset Purchase Agreement and related agreements. During the year ended December 31, 2023, the Company recognized $14.0 million of deferred revenue – related party in connection with the Collaboration Agreement as license revenue.

During the year ended December 31, 2024, $33.3 million of service revenue, inclusive of the $14.0 million of deferred revenue – related party recognized as service revenue, was recognized based on cumulative progress of PPQ services under the Asset Purchase Agreement and related agreements. During the year ended December 31, 2023, the Company recognized $70.4 million related to the reimbursement of research and development expenses under the Collaboration Agreement, which were recorded as an offset to research and development expenses.

Debt Financing

On August 2, 2022 the Company, as borrower, and Meira UK II and Meira Ireland, as guarantors (the "Subsidiary Guarantors"), entered into a senior secured financing arrangement (the "Financing Agreement") by and among the Company, the Subsidiary Guarantors, the lenders and other parties from time to time party thereto and Perceptive Credit Holdings III, LP, as administrative agent and lender ("Perceptive"). On December 19, 2022, the Financing Agreement was converted to a notes purchase agreement and guaranty (the "Notes Purchase Agreement") between the same parties and under substantially the same terms and conditions as the Financing Agreement, subject to certain customary note constitution terms. Perceptive Advisors, LLC, an affiliate of Perceptive, is a 16.0% holder of the ordinary shares of the Company. Additionally, Ellen Hukkelhoven, Ph.D., a director of the Company, is an employee of Perceptive Advisors, LLC. Refer to the discussion in Note 13 for further information related to the accounting for the debt financing.

May 2023 Private Placement

On May 3, 2023, the Company issued 10,773,913 ordinary shares in a private placement for gross proceeds of $62.0 million, excluding offering costs of approximately $4.1 million. Perceptive Advisors, LLC and Adage Capital Partners, L.P. a greater than 5% holder of the ordinary shares of the Company, purchased 4,347,826 and 1,565,217 of the ordinary shares, respectively, issued on the same terms and conditions as the other investors in the offering.

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 $5.6 million and $5.5 million for the years ended December 31, 2024 and 2023, respectively.

Eight clinical trial site leases were assigned to Johnson & Johnson Innovative Medicine during the year ended December 31, 2024 in connection with the Asset Purchase Agreement and related agreements. There were no leases recognized during the years ended December 31, 2024 and 2023.

The components of lease cost for the years ended December 31, 2024 and 2023 are as follows (in thousands):

	Years Ended December 31,	
	2024	2023
Finance lease cost		
Amortization of right-of-use assets	$ 981	$ 1,124
Total finance lease cost	981	1,124
Operating lease cost	5,630	5,473
Short-term lease cost	256	159
Total lease cost	$ 6,867	$ 6,756

Amounts reported in the consolidated balance sheets for leases where the Company is the lessee as of December 31, 2024 and 2023 were as follows (in thousands):

	December 31, 2024	December 31, 2023
Operating leases		
Right-of-use assets	$ 10,576	$ 15,910
Capitalized lease obligations	$ 11,576	$ 17,145
Finance leases		
Right-of-use assets	$ 22,198	$ 24,432
Weighted-average remaining lease term		
Operating leases	3.6 years	4.3 years
Finance leases	173.9 years	174.8 years
Weighted-average discount rate		
Operating leases	8.8 %	8.8 %
Finance leases	8.0 %	8.0 %

Other information related to leases as of the years ended December 31, 2024 and 2023 are as follows (in thousands):

	Years Ended December 31,	
	2024	2023
Cash paid for amounts included in the measurement of lease liabilities		
Operating cash flows from operating leases	$ 5,408	$ 5,662

Future minimum lease payments under non-cancellable leases as of December 31, 2024 are as follows (in thousands):

	Operating Leases
2025	$ 4,936
2026	5,078
2027	1,428
2028	1,238
2029	541
Total undiscounted lease payments	$ 13,221
Less: Imputed interest	(1,645)
Total lease liabilities	$ 11,576

13. Debt Financing

On August 2, 2022 the Company, and the Subsidiary Guarantors, entered into the Financing Agreement with Perceptive. On December 19, 2022, the Financing Agreement was converted to a Notes Purchase Agreement between the same parties and under substantially the same terms and conditions as the Financing Agreement, subject to certain customary note constitution terms. The Company and the Subsidiary Guarantors entered into a Consent and Amendment with Perceptive on August 10, 2023 (the "First Consent and Amendment), and the Company and the Subsidiary Guarantors entered into a second Consent and Amendment with Perceptive on December 20, 2023 (the "Second Consent and Amendment").

The Notes Purchase Agreement provides for an initial $75.0 million notes issuance (the "Tranche 1 Notes"). Pursuant to the First Consent and Amendment, the Company was able to request in its sole discretion, and Perceptive agreed to subscribe to purchase upon such request, an additional $25.0 million notes issuance (the "Tranche 2 Notes") at any time before August 2, 2024 subject to the terms of the Notes Purchase Agreement. Previously, the Company's request for issuance of the Tranche 2 Notes was to be determined at Perceptive's sole discretion. The Notes Purchase Agreement matures on August 2, 2026 and is interest-only during the term. The Company has the option to redeem outstanding principal notes at any time along with an applicable early redemption fee. Under each of the First Consent and Amendment and the Second Consent and Amendment, the Notes Purchase Agreement was amended to increase the applicable early redemption fee. Outstanding amounts under the Notes Purchase Agreement bear interest at a fluctuating rate per annum equal to 10.00% plus the secured overnight financing rate administered by the Federal Reserve Bank of New York for a one-month tenor, subject to a 1.00% floor. The annual interest rate was 14.85% at December 31, 2024. As of December 31, 2024, the outstanding balance of the Tranche 1 Notes was $75.0 million plus interest payable of $2.9 million. During the years ended December 31, 2024 and 2023, the Company recorded interest expense of $11.6 million and $11.3 million, respectively.

The Company's obligations under the Notes Purchase Agreement are secured by the Company's London, UK and Shannon, Ireland manufacturing facilities, $3.0 million of the Company's cash and the bank accounts of the Subsidiary Guarantors, and the issued and outstanding equity interests of the Subsidiary Guarantors.

The Notes Purchase Agreement imposes certain covenants and restrictions on the Company and the Subsidiary Guarantors, including restrictions pertaining to: (i) the incurrence of additional indebtedness, (ii) limitations on liens, (iii) limitations on certain investments, (iv) making distributions, dividends and other payments, (v) mergers, consolidations and acquisitions, (vi) dispositions of assets, (vii) the Company's maintenance of at least $3.0 million in a U.S. bank account, (viii) transactions with affiliates, (ix) changes to governing documents, (x) changes to certain agreements and leases and (xi) changes in control; however, certain of these restrictions contain exceptions which allow the Company to license, sell and monetize assets in its AAV-hAQP1 program in development to treat radiation-induced xerostomia, its AAV-GAD program in development to treat Parkinson's disease and its gene regulation platform technologies. As of December 31, 2024, the Company is in compliance with all covenants.

In connection with entering into the Financing Agreement, the Company granted warrants to Perceptive to purchase up to (i) 400,000 ordinary shares of the Company at an exercise price of $15.00 per share and (ii) 300,000 ordinary shares of the Company at an exercise price of $20.00 per share. The warrants are exercisable immediately and expire on August 2, 2027. The Company recorded a debt discount of $2.3 million for the allocated fair value of the warrants.

The Company also capitalized certain lender and legal costs associated with the Notes Purchase Agreement totaling $2.1 million, which were recorded as a discount to the loan. The aggregate discount of $4.4 million is being amortized to interest expense over the term of the Notes Purchase Agreement. The Company amortized $1.1 million of the discount to interest expense during each of the years ended December 31, 2024 and 2023. At December 31, 2024, the remaining unamortized discount was $1.8 million.

14. Commitments and Contingencies

There were no new material commitments or contingencies entered into during the year ended December 31, 2024.

15. 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 required to contribute 0.5%, to meet minimum legal pension funding levels of 8%, but may make optional contributions up to the annual allowance HMRC limits.

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.

Belgium

Meira Belgium operates a defined contribution pension plan. All eligible employees receive an employer pension contribution of 8% of their annual salary. Employees do not make contributions to the plan.

During each of the years ended December 31, 2024 and 2023, employer contributions to all plans were $2.5 million.

16. Subsequent Event

Hologen Transactions

On March 9, 2025 (the "Signing Date"), the Company and its affiliates entered into a strategic collaboration with Hologen Limited, a non-cellular company limited by shares incorporated in Guernsey ("Hologen"), and its affiliates. Hologen is a leading developer of multi-modal generative AI foundation models of real-world clinical data for clinical medicine and pharmaceutical drug development. Hologen emerged as a spin-out from University College London and Kings College London. As part of the strategic collaboration, the Company and Hologen have entered into the Framework Agreements (as defined below), pursuant to which the Company and its affiliates will receive from Hologen an upfront cash payment of $200 million (the "Upfront Payment") on the Closing Date (as defined below), and Hologen will provide additional funding of up to an additional $230 million as further described below. As part of the strategic collaboration, the Company also received 250,000 Class A shares of Hologen at a nominal price. Furthermore, the Company has the option to receive up to an additional 500,000 Class A shares of Hologen at a nominal price if certain funding obligations as described herein are not met by Hologen. Each of Dr. Forbes and Mr. Giroux received a nominal equity interest in Hologen and are, respectively, members of Hologen's Scientific Advisory Board and Advisory Board.

The closing of the transactions contemplated by the Framework Agreements (the "Closing Date") is expected to occur in the second calendar quarter of 2025, subject to customary closing and funding conditions, including the receipt of the clearances and approvals applicable to the proposed transactions under the foreign direct investment laws of the United Kingdom and the satisfaction or waiver of certain other closing conditions.

Neuro Framework Agreement

On the Signing Date, the Company, MeiraGTx Neuro UK Limited, a private company limited by shares incorporated in England and a wholly-owned subsidiary of the Company ("MeiraGTx Neuro UK"), Hologen Neuro AI Limited, a non-cellular company limited by shares incorporated in Guernsey and an affiliate of Hologen ("Hologen Neuro"), and Hologen, entered into that certain Framework Agreement (the "Neuro Framework Agreement"), pursuant to which, on the Closing Date, the Company, MeiraGTx Neuro UK, MeiraGTx Neuro I, LLC, a Delaware limited liability company and a wholly-owned subsidiary of the Company ("MeiraGTx Neuro US"), Hologen, Hologen Neuro and Hologen Neuro AI UK Limited, a private company limited by shares incorporated in England and an affiliate of Hologen ("Hologen Neuro UK"), shall enter into a Collaboration and License Agreement (the "Collaboration Agreement") for the research, development, manufacture and commercialization of the Company's (i) AAV-GAD investigational gene therapy for the treatment of Parkinson's disease, AAV-BDNF investigational gene therapy for the treatment of genetic obesity disorders and other potential locally delivered genetic medicines to the central nervous system (the "Clinical Programs") and (ii) proprietary device designed to effect the local delivery of a gene therapy product into the central nervous system or any

topographic or subcutaneous tissue modification on the face and scalp, of humans or animals (the "Delivery Device"), in each case, in accordance with the terms and conditions of the Collaboration Agreement.

On the Closing Date, under the Collaboration Agreement, MeiraGTx Neuro US will receive the applicable portion of the Upfront Payment in consideration for granting to Hologen Neuro and Hologen Neuro UK, as of the Closing Date and subject to the license granted by Hologen Neuro and Hologen Neuro UK back to MeiraGTx Neuro UK, exclusive, worldwide, royalty-free, fully paid-up licenses to certain of the Company's intellectual property rights for the research, development, manufacture and commercialization of the Clinical Programs and the Delivery Device. On the Closing Date, (a) MeiraGTx Neuro UK will receive Class A shares of Hologen Neuro representing a 30% ownership of the issued share capital of Hologen Neuro, in consideration for the provision of services to Hologen Neuro and Hologen Neuro UK as specified in the Collaboration Agreement, including services relating to the development of the Clinical Programs and the Delivery Device and certain other transition services, and (b) Hologen Guernsey will receive Class B shares of Hologen Neuro representing a 70% ownership of the issued share capital of Hologen Neuro, in consideration for paying the applicable portion of the Upfront Payment to MeiraGTx Neuro US, as well as a commitment to provide additional capital of up to $230 million to fund the development of the Clinical Programs and the Delivery Device. Additionally, Hologen will license to Hologen Neuro its proprietary multi-modal generative foundation models (LMMs), or large medicine models, pursuant to a license agreement mutually agreeable to the parties.

As of the Closing Date, Hologen Neuro shall be governed by a board of directors comprised of three representatives designated by Hologen and two representatives designated by MeiraGTx Neuro UK, and certain material business decisions (as further enumerated in the Neuro Framework Agreement) will require the approval of at least 70% of the directors then in office.

Following the Closing Date and in accordance with the terms of the Collaboration Agreement, the parties shall negotiate in good faith and enter into clinical and commercial supply agreements, pursuant to which MeiraGTx Neuro UK (directly, or through affiliates or subcontractors) shall manufacture and supply AAV-GAD, AAV-BDNF and other potential locally delivered genetic medicines to the central nervous system.

Manufacturing Framework Agreement

On the Signing Date, MeiraGTx Manufacturing Limited, a private company limited by shares incorporated in England and a wholly-owned subsidiary of the Company ("MeiraGTx Manufacturing"), MeiraGTx Limited, a private company limited by shares incorporated in England and a wholly-owned subsidiary of the Company ("MeiraGTx Limited"), and Hologen, entered into that certain Framework Agreement (the "Manufacturing Framework Agreement" and, together with the Neuro Framework Agreement, the "Framework Agreements"), pursuant to which, on the Closing Date and in exchange for the applicable portion of the Upfront Payment, Hologen will acquire a minority interest in MeiraGTx Manufacturing, an entity that will comprise the Company's flexible and scalable end-to-end genetic medicines manufacturing business, which is solely run by MeiraGTx Manufacturing and MeiraGTx Limited prior to the Closing Date. Hologen will also contribute a portion of the annual funding to MeiraGTx Manufacturing.

As of the Closing Date, MeiraGTx Manufacturing shall be governed by a board of directors comprised of three representatives designated by MeiraGTx Limited and two representatives designated by Hologen, and certain material business decisions (as further enumerated in the Manufacturing Framework Agreement) will require the approval of at least 70% of the directors then in office.

For a period of twelve months following the Closing Date, Hologen has an exclusive, irrevocable option to purchase additional shares in MeiraGTx Manufacturing at a specified price, such that following exercise of such option, Hologen shall own 40% of the issued share capital of MeiraGTx Manufacturing in the aggregate. In the event that Hologen does not exercise its option, MeiraGTx has an exclusive, irrevocable option to purchase all of the shares of MeiraGTx Manufacturing held by Hologen for the same price that Hologen paid for such shares. Such option shall be exercisable anytime beginning on the third anniversary of the Closing Date and ending three years thereafter.

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, 2024. 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, 2024.

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 a "smaller reporting company" as defined under SEC rules.

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, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

During the three months ended December 31, 2024, none of our directors or "officers" (as defined in Rule 16a-1(f) under the Exchange Act) adopted, modified or terminated a "Rule 10b5-1 trading arrangement" and/or "non-Rule 10b5-1 trading arrangement," as each term is defined in Item 408(a) of Regulation S-K.

On March 13, 2025, our Board of Directors approved a waiver under the Company's Code of Business Conduct and Ethics for Alexandria Forbes, Ph.D., President and Chief Executive Officer, approving Dr. Forbes' participation on the Scientific Advisory Board of Hologen Limited and subscription of 100,000 shares of Hologen Limited for a nominal amount.

On March 13, 2025, our Board of Directors approved a waiver under the Company's Code of Business Conduct and Ethics for Richard Giroux, Chief Financial Officer and Chief Operating Officer, approving Mr. Giroux's participation on the Advisory Board of Hologen Limited and subscription of 50,000 shares of Hologen Limited for a nominal amount.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

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 2025 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2024.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item is incorporated by reference to our definitive proxy statement for our 2025 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2024.

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, 2024)

The following table provides information as of December 31, 2024 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)	1,146,847	$ 5.26	—
2018 Plan (2) (3)	11,610,490	$ 13.76	300,888
2018 ESPP (4)	—	—	3,159,113
Equity compensation plans not approved by shareholders	—	—	—
Total	12,757,337	$ 12.57	3,460,001

(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, 2024 there were a total of 4,252,250 shares subject to restricted share units included in the Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights. Deferred share units received by certain non-employee directors are fully vested and non-forfeitable and were not taken into account in the foregoing calculation.

(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 2025 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2024.

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 2025 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2024.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this Item is incorporated by reference to our definitive proxy statement for our 2025 annual shareholder meeting to be filed with the SEC within 120 days of the fiscal year ended December 31, 2024.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
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	
4.4	Form of Warrant Agreement, dated August 2, 2022, issued by MeiraGTx Holdings plc to certain warrant holders.	10-Q	001-38520	4.1	11/10/22	
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-Q	001-38520	10.1	08/12/24	
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	
10.11#	2018 Employee Share Purchase Plan.	S-1/A	333-224914	10.15	5/29/18	

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
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-K	001-38520	10.14	3/11/21	
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	
10.23†	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	
10.24††	Collaboration, Option and License Agreement, dated January 30, 2019, by and among Janssen Pharmaceuticals, Inc., MeiraGTx UK II Limited and MeiraGTx Holdings plc.					*
10.25††	First Amendment to Collaboration, Option and License Agreement, dated December 16, 2021.	10-K	001-3852	10.26	3/10/22	

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
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	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	
10.28#	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	
10.29#	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	
10.30	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	
10.31	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	
10.32#	Deferred Compensation Plan for Non-Employee Directors.	10-K	001-38520	10.35	3/10/22	
10.33#	Form of Restricted Share Unit Grant Notice and Restricted Share Unit Agreement for Non-Employee Directors Under the 2018 Incentive Award Plan.	10-K	001-38520	10.36	3/10/22	
10.34††	Credit Agreement and Guaranty, dated August 2, 2022, by and among MeiraGTx Holdings plc, as borrower, MeiraGTx UK II Limited and MeiraGTx Ireland DAC, as guarantors, the lenders and other parties from time to time party thereto and Perceptive Credit Holdings III, LP, as administrative agent and lender.	10-Q	001-38520	10.1	11/10/22	

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
10.35	Amendment No. 1 to Credit Agreement and Guaranty, dated December 19, 2022, by and among MeiraGTx Holdings plc, as borrower, certain subsidiary guarantors and lenders party thereto, and Perceptive Credit Holdings III, LP, as administrative agent.	10-K	001-38520	10.36	3/14/23	
10.36††	Amended and Restated Notes Purchase Agreement and Guaranty, dated December 19, 2022, by and among MeiraGTx Holdings plc, as issuer, the subsidiary guarantors and noteholders from time to time party thereto, and Perceptive Credit Holdings III, LP, as administrative agent.	10-K	001-38520	10.37	3/14/23	
10.37	Tranche 1 Note, dated December 19, 2022, by and among MeiraGTx Holdings plc, as issuer, the subsidiaries guarantors and noteholders from time to time party thereto, and Perceptive Credit Holdings III, LP, as administrative agent.	10-K	001-38520	10.38	3/14/23	
10.38	Consent and Amendment to Amended and Restated Notes Purchase Agreement and Guaranty, dated August 10, 2023, by and among MeiraGTx Holdings plc, as issuer, the subsidiary guarantors and noteholders from time to time party thereto, and Perceptive Credit Holdings III, LP, as administrative agent and noteholder.	8-K	001-38520	10.1	8/10/23	
10.39	Consent and Amendment to Amended and Restated Notes Purchase Agreement and Guaranty, dated December 20, 2023, by and among MeiraGTx Holdings plc, as issuer, the subsidiary guarantors and noteholders from time to time party thereto, and Perceptive Credit Holdings III, LP, as administrative agent and noteholder.	10-K	001-38520	10.39	3/15/24	
10.40	Securities Purchase Agreement, dated November 9, 2022, by and among MeiraGTx Holdings plc and Johnson & Johnson Innovation – JJDC, Inc.	10-K	001-38520	10.39	3/14/23	
10.41	Registration Rights Agreement, dated November 15, 2022, by and among MeiraGTx Holdings plc and Johnson & Johnson Innovation – JJDC, Inc.	10-K	001-38520	10.40	3/14/23	
10.42	First Amendment to Registration Rights Agreement, dated May 12, 2023, by and among MeiraGTx Holdings plc and Johnson & Johnson Innovation – JJDC, Inc.	10-Q	001-38520	10.3	8/10/23	
10.43	Securities Purchase Agreement, dated May 3, 2023, by and among MeiraGTx Holdings plc and the Investors named therein.	S-3	333-273672	10.1	8/3/23	
10.44	Registration Rights Agreement, dated May 5, 2023, by and among MeiraGTx Holdings plc and the Investors named therein.	S-3	333-273672	10.2	8/3/23	

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
10.45	Investment Agreement, dated October 30, 2023, by and among MeiraGTx Holdings plc, Sanofi Foreign Participations B.V. and Sanofi.	8-K	001-38520	10.1	10/30/23	
10.46	Registration Rights Agreement, dated October 30, 2023, by and between MeiraGTx Holdings plc and Sanofi Foreign Participations B.V.	8-K	001-38520	10.2	10/30/23	
10.47††	Asset Purchase Agreement, dated December 20, 2023, by and among Janssen Pharmaceuticals, Inc., MeiraGTx UK II Limited and MeiraGTx Holdings plc.	10-K	001-38520	10.47	3/15/24	
10.48††	Termination Agreement, dated December 20, 2023, by and among Janssen Pharmaceuticals, Inc., MeiraGTx UK II Limited and MeiraGTx Holdings plc.	10-K	001-38520	10.48	3/15/24	
10.49††	Framework Agreement, dated March 9, 2025, by and among Hologen Limited, Hologen Neuro AI Limited, MeiraGTx Neuro UK Limited and MeiraGTx Holdings plc.					*
10.50††	Form of Collaboration and License Agreement by and among Hologen Neuro AI Ltd, Hologen Neuro AI UK Limited, Hologen Limited, MeiraGTx Holdings plc, MeiraGTx UK Neuro Limited and MeiraGTx Neuro I, LLC.					*
10.51††	Framework Agreement, dated March 9, 2025, by and among MeiraGTx Manufacturing Limited, MeiraGTx Limited and Hologen Limited.					*
19.1	MeiraGTx Holdings plc Insider Trading Compliance Policy.					*
21	List of Subsidiaries.					*
23.1	Consent of Ernst & Young LLP.					*
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14(a)/15d-14(a) under the Securities Exchange Act of 1934, as amended.					*
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14(a)/15d-14(a) under the Securities Exchange Act of 1934, as amended.					*
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					**

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Form	File No.	Exhibit	Filing Date	Filed/ Furnished Herewith
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.					**
97.1	Policy for Recovery of Erroneously Awarded Compensation.	10-K	001-38520	97.1	3/15/24	
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
†† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K

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 13, 2025

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 13, 2025
/s/ Richard Giroux Richard Giroux	Chief Financial Officer (Principal Financial and Accounting Officer)	March 13, 2025
/s/ Keith R. Harris, Ph.D. Keith R. Harris, Ph.D.	Chairman of the Board and Director	March 13, 2025
/s/ Ellen Hukkelhoven, Ph.D. Ellen Hukkelhoven, Ph.D.	Director	March 13, 2025
/s/ Lord Mendoza Lord Mendoza	Director	March 13, 2025
/s/ Nicole Seligman Nicole Seligman	Director	March 13, 2025
/s/ Thomas E. Shenk, Ph.D. Thomas E. Shenk, Ph.D.	Director	March 13, 2025
/s/ Debra Yu, M.D. Debra Yu, M.D.	Director	March 13, 2025