UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended March 31, 2021

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 001-37418

Sio Gene Therapies Inc.

(Exact name of registrant as specified in its charter)

Delaware	**85-3863315**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
130 West 42nd St., 26th Floor New York, New York	**10036**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(877) 746-4891**

Axovant Gene Therapies Ltd.
Suite 1, 3rd Floor
11-12 St. James's Square
London SW1Y 4LB, United Kingdom

(Former name, former address and former fiscal year, if changed since last report)

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

Title of each Class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.00001 per share	SIOX	The Nasdaq Stock Market LLC

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

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

Indicate by check mark whether the registrant is not required to file reports pursuant to Section 13 or 15(d) of the 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. (Check one):

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 7(a)(2)(B) of the Securities Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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

The aggregate market value of voting shares of common stock held by non-affiliates of the registrant at the end of the registrant's most recently completed second fiscal quarter ended September 30, 2020 was approximately $131,913,331 based on the last reported sale price of the shares of common stock on The Nasdaq Global Select Market on September 30, 2020 of $4.62 per share.

The number of shares outstanding of the Registrant's common stock, $0.00001 par value per share, on June 7, 2021, was 69,558,434.

SIO GENE THERAPIES INC.

ANNUAL REPORT ON FORM 10-K
FOR THE FISCAL YEAR ENDED MARCH 31, 2021

TABLE OF CONTENTS

Summary of the Material Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties that you should be aware of in evaluating our business. These risks include, but are not limited to, the following:

- Our business, operations and clinical development plans and timelines could continue to be adversely impacted by the effects of health epidemics, including the recent COVID-19 pandemic, on the manufacturing, clinical trial and other business activities performed by us or by third parties with whom we conduct business, including our contract manufacturers, contract research organizations, or CROs, shippers and others.
- We have a limited operating history and have never generated any product revenues.
- We are heavily dependent on the success of our gene therapy product candidates, which are still in early stages of clinical or preclinical development. If we are unable to successfully develop and commercialize any of our product candidates, our business will be harmed.
- We may be required to make significant payments to third parties under the agreements pursuant to which we acquired our gene therapy product candidates.
- Gene therapies are novel, complex, difficult and expensive to manufacture. We do not have our own manufacturing capabilities and will rely on third parties to produce clinical and commercial supplies of our product candidates. Delays in manufacturing processes, including recently at Oxford, may result in delays in our planned clinical trials that would otherwise harm our business and prospects.
- Our business plan may lead to the initiation of one or more gene therapy development programs, the discontinuation of one or more development programs, or the execution of one or more transactions that you do not agree with or that you do not perceive as favorable to your investment.
- Clinical trials are expensive, time-consuming, difficult to design and implement and involve an uncertain outcome.
- If we are not able to obtain required regulatory approvals, we will not be able to commercialize our gene therapy product candidates, and our ability to generate revenue will be materially impaired.
- The intended tax effects of our corporate structure prior to and following the Domestication (as defined below) and our corporate reorganization to align our corporate structure with current and future business activity (the "Reorganization"), and intercompany arrangements prior to the Domestication and Reorganization, depend on the application of the tax laws of various jurisdictions and on how we operate our business.
- We expect to incur significant losses for the foreseeable future and may never achieve or maintain profitability.
- We will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of our product candidates.
- Interim "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- Our gene therapy product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.
- Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.
- 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, even if approved.
- If the market opportunities for any product candidates we may develop are smaller than we believe they are, our revenues, if any, may be adversely affected, and our business may suffer. Because the target patient populations for many of the product candidates we may develop are small, we must be able to successfully identify patients and achieve a significant market share to achieve and maintain profitability and growth.

- We face significant competition from other biotechnology and pharmaceutical companies, 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 and our operating results will suffer if we fail to compete effectively.
- We may not be able to protect our intellectual property rights throughout the world, which could impair our business.
- Third-party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights may delay or prevent the development and commercialization of our product candidates.
- The market price of our common stock has been and is likely to continue to be highly volatile, and you may lose some or all of your investment.

The summary risk factors described above should be read together with the text of the full risk factors below, in the section titled "Risk Factors" in Part I, Item 1A. and the other information set forth in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes, as well as in other documents that we file with the Securities and Exchange Commission. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us, or that we currently deem to be immaterial may also harm our business, financial condition, results of operations and future growth prospects.

PART I.

Cautionary Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements are often identified by the use of words such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "project," "will," "would" or the negative or plural of these words or similar expressions or variations, although not all forward-looking statements contain these identifying words. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur and actual results could differ materially from those projected in the forward-looking statements.

The forward-looking statements appearing in a number of places throughout this Annual Report on Form 10-K include, but are not limited to, statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things:

- the success and timing of our ongoing development and potential commercialization of our product candidates;
- our relationships under our license agreements;
- the success of our interactions with the U.S. Food and Drug Administration ("FDA") and international regulatory authorities;
- the anticipated start dates, durations and completion dates of our ongoing and future nonclinical studies and clinical trials, as well as subsequent portions or cohorts of our ongoing clinical trials;
- the receipt of approvals or endorsements by data monitoring or other committees necessary for commencement or continuation of clinical trials;
- the anticipated designs of our future clinical studies;
- anticipated future regulatory submissions and the timing of, and our ability to, obtain and maintain regulatory approval for our product candidates;
- the rate and degree of market acceptance and clinical utility of any approved product candidate;
- our ability to identify and in-license or acquire additional product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- continued service of our executive officers or other key scientific or management personnel;
- our ability to obtain, maintain and enforce intellectual property rights for our product candidates;
- our anticipated future cash position;
- our estimates regarding our results of operations, financial condition, liquidity, capital requirements, prospects, growth and strategies;
- our ability to maintain and operate our business in light of the COVID-19 pandemic;
- the success of competing therapies that are or may become available; and
- our stated objective of building the world's leading gene therapy company for the treatment of neurological diseases.

We have based these forward-looking statements largely on our current expectations and projections about future events, including the responses we expect from the FDA and other regulatory authorities and financial trends that we believe may affect our financial condition, results of operations, business strategy, nonclinical studies and clinical trials and financial needs. Such forward-looking statements are subject to a number of risks, uncertainties, assumptions and other factors known and unknown that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified herein, and those discussed in the section titled "Risk Factors" set forth in Part I, Item 1A of this Annual Report on Form 10-K and in our other filings with the U.S. Securities and Exchange Commission ("SEC"). These risks are not exhaustive. You should not rely upon forward-looking statements as predictions of future events. Furthermore, such forward-looking statements speak only as of the date of this report. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Except as required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date of such statements.

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 report, 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 potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements as predictions of future events.

In November 2020, Axovant Gene Therapies Ltd. changed its jurisdiction of incorporation from Bermuda to Delaware and changed its corporate name to Sio Gene Therapies Inc., which we refer to collectively as the Domestication. Unless the context requires otherwise, references in this report to "Sio", the "Company," "we," "us," and "our" refer to (i) Axovant Gene Therapies Ltd. and its subsidiaries prior to the Domestication and (ii) Sio Gene Therapies Inc. and its subsidiaries after the Domestication. In addition, all references to "common stock" before the Domestication refer to the common shares of Axovant Gene Therapies Ltd., and all such references after the Domestication refer to the common stock of Sio.

Item 1. Business

Overview

We are a clinical-stage company focused on developing gene therapies to radically transform the lives of patients with neurodegenerative diseases. We currently have three clinical-stage programs: (i) the AXO-AAV-GM1 program for the treatment of GM1 gangliosidosis in which five patients have been dosed in the late-infantile/juvenile (Type II) low-dose cohort of stage 1, and we have dosed two late-infantile/juvenile (Type II) patients in the higher dose cohort of the study and expect to continue to dose Type II patients and initiate the low-dose infantile (Type I) patients in calendar year 2021; (ii) the AXO-AAV-GM2 program for the treatment of GM2 gangliosidosis (including Tay-Sachs and Sandhoff diseases) for which we received clearance for the IND from the FDA in November 2020, and in which we dosed the first infantile patient in January 2021; and (iii) the AXO-Lenti-PD program for the treatment of Parkinson's disease, comprised of the ProSavin Phase 1/2 study in which 15 patients were previously dosed and the AXO-Lenti-PD SUNRISE-PD study in which we have dosed two patients in Cohort 1 of the dose-escalation study and four patients in Cohort 2.

We are dedicated to realizing the potential of gene therapies to offer transformative patient outcomes in areas of high unmet medical need and extending the reach of gene therapies to highly prevalent neurodegenerative disorders like Parkinson's disease. We have assembled a portfolio of gene therapies in partnership with leading scientific institutions and have built a team with extensive experience in the gene therapy space. Our team pursues new innovations in vector design and delivery to optimize our investigational gene therapy products for safety, potency, durability, and immunologic response. We will continue to build integrated internal development capabilities from product development through commercialization and focus on accelerating the pace of product development in the clinic. As part of our ongoing business strategy, we continue to explore potential opportunities to acquire or license new product candidates as well as opportunities for partnership or collaboration on our existing products in development. Our vision is to build the world's leading gene therapy company for the treatment of neurodegenerative diseases by progressing our current programs and identifying, developing and commercializing other novel gene therapy treatments for neurodegenerative diseases.

The Domestication

We have substantially completed our previously disclosed corporate transformation to align corporate structure and governance with current and future business activity, including significantly reducing the number of our subsidiaries. On November 12, 2020, Axovant Gene Therapies Ltd. ("AGT") discontinued as a Bermuda exempted company pursuant to Section 132G of the Companies Act 1981 of Bermuda, and pursuant to Section 388 of the General Corporation Law of the State of Delaware (the "DGCL"), continued its existence under the DGCL as a corporation named Sio Gene Therapies Inc. ("Sio") organized in the State of Delaware. The Domestication effected a change in our jurisdiction of incorporation, and other changes of a legal nature, including changes in our organizational documents. Our consolidated business, operations, assets and liabilities did not change upon effectiveness of the Domestication. However, following the Domestication, the principal executive offices and registered offices of Sio are located at 130 West 42nd St, 26th Floor, New York, New York 10036, and the telephone number for Sio at its principal executive offices is 1 (877) 746-4891. The fiscal year end of Sio Gene Therapies Inc. following the Domestication remains at March 31. In addition, our directors and executive officers immediately after the Domestication were the same individuals who were directors and executive officers, respectively, immediately prior to the Domestication.

In the Domestication, each of our currently issued and outstanding common shares automatically converted by operation of law, on a one-for-one basis, into shares of Sio common stock. Consequently, upon the effectiveness of the Domestication, each holder of an AGT common share instead holds a share of Sio common stock representing the same proportional equity interest in Sio as that shareholder held in AGT and representing the same class of shares. The number of shares of Sio common stock outstanding immediately after the Domestication is the same as the number of common shares of AGT. outstanding immediately prior to the Domestication. In connection with the Domestication, we adopted a new certificate of incorporation, bylaws and form of common stock certificate, copies of which were filed as Exhibits 3.1, 3.2 and 4.1, respectively, to our Report on Form 8-K12G3 filed with the SEC on November 13, 2020.

Our Product Pipeline

The following table summarizes the status of our gene therapy development programs, for which we hold global commercial rights to each:

Gene Therapy Program	Clinical Indication	Clinical Development Stage
AXO-AAV-GM1	GM1 gangliosidosis	Phase 1/2
AXO-AAV-GM2	GM2 gangliosidosis (including Tay-Sachs and Sandhoff diseases)	Phase 1/2
AXO-Lenti-PD	Parkinson's disease	Phase 2

AXO-AAV-GM1 and AXO-AAV-GM2 Programs

Overview

We are developing AXO-AAV-GM1 and AXO-AAV-GM2 as potential one-time disease-modifying treatments for GM1 and GM2 gangliosidosis (including Tay-Sachs disease and Sandhoff disease), respectively.

GM1 Gangliosidosis and GM2 Gangliosidosis (Including Tay-Sachs and Sandhoff Diseases)

GM1 gangliosidosis is a rare, inherited neurodegenerative lysosomal storage disorder characterized by the accumulation of GM1 ganglioside. This accumulation occurs due to a defect in the galactosidase beta 1 ("*GLB1*") gene. The *GLB1* gene codes for the β-galactosidase ("β-gal") enzyme which catalyzes the hydrolysis of GM1 gangliosides. Impaired β-gal activity results in the toxic accumulation of GM1 gangliosides, causing the progressive destruction of nerve cells in the brain and spinal cord and early death. GM1 gangliosidosis is uniformly fatal, and there are no disease-modifying treatment options. The estimated incidence for GM1 gangliosidosis is approximately one in 100,000 live births worldwide. In 2019, we collaborated with the National Institutes of Health ("NIH") to publish a comprehensive retrospective study characterizing the natural history of Type I GM1 gangliosidosis in *Molecular Genetics and Metabolism* (Lang et.al., 2019). This paper describes a rapidly progressive clinical course of Type I GM1 gangliosidosis, in which almost all patients experience significant multi-organ system dysfunction and neurodevelopmental regression between six and 18 months of age.

GM2 gangliosidosis, also known as Tay-Sachs or Sandhoff diseases, is a rare, inherited neurodegenerative lysosomal storage disorder characterized by buildup of GM2 ganglioside in lysosomes. Defects in the hexosaminidase subunit alpha ("*HEXA*") gene (leading to Tay-Sachs disease) and hexosaminidase subunit beta ("*HEXB*") gene (leading to Sandhoff disease) cause deficiencies in beta-hexosaminidase A ("Hex A") enzyme activity. Hex A enzyme deficiency leads to progressive accumulation of GM2 gangliosides in the central nervous system ("CNS") with ensuing neurodegeneration. Both Tay-Sachs disease and Sandhoff disease are characterized by progressive nervous system dysfunction, resulting in marked cognitive and physical impairment. Tay-Sachs and Sandhoff diseases result in approximately 50% mortality by three and a half years of age and 75% mortality by five years of age. Currently there are no disease-modifying treatment options for either Tay-Sachs disease or Sandhoff disease, and management is limited to symptomatic treatment. The estimated incidence for Tay-Sachs and Sandhoff diseases is approximately one in 150,000 live births worldwide.

The estimated incidence for the combination of GM1 gangliosidosis, Tay-Sachs and Sandhoff diseases is approximately one in 60,000 live births worldwide. We estimate that there are between approximately 600 and 1,000 patients with GM1 gangliosidosis, Tay-Sachs and Sandhoff diseases in the United States and European Union combined. These diseases, in the severe form, reduce life expectancy to two to four years.

AXO-AAV-GM1

AXO-AAV-GM1 is an investigational gene therapy currently being developed as a potential one-time disease modifying treatment for GM1 gangliosidosis. The program utilizes an adeno-associated virus ("AAV") vector to deliver a functional copy of the *GLB1* gene with the goals of restoring β-gal enzyme activity both systematically and in the CNS, reducing GM1 ganglioside accumulation to ultimately improve neurological function and peripheral manifestations, such as cardiac and skeletal abnormalities, and thereby extend survival. The therapy is administered intravenously and utilizes the AAV9 capsid, which has been shown to cross the blood-brain barrier. Intravenous administration has the potential to broadly transduce the CNS and peripheral tissues, as well as treat peripheral manifestations of the disease. We licensed exclusive worldwide rights for the development and commercialization of AXO-AAV-GM1 from UMMS in December 2018. In November 2019, we announced that the FDA had granted orphan drug designation for AXO-AAV-GM1.

Preclinical studies in GM1 murine and feline models have demonstrated that AXO-AAV-GM1 increases β-gal enzyme activity, reduces GM1 ganglioside accumulation, improves neuromuscular function, and extends survival. Magnetic resonance imaging ("MRI") of GM1 feline models treated with other GM1 gene therapy demonstrated substantially normal brain architecture through at least two years of age, as compared with untreated GM1 feline models.

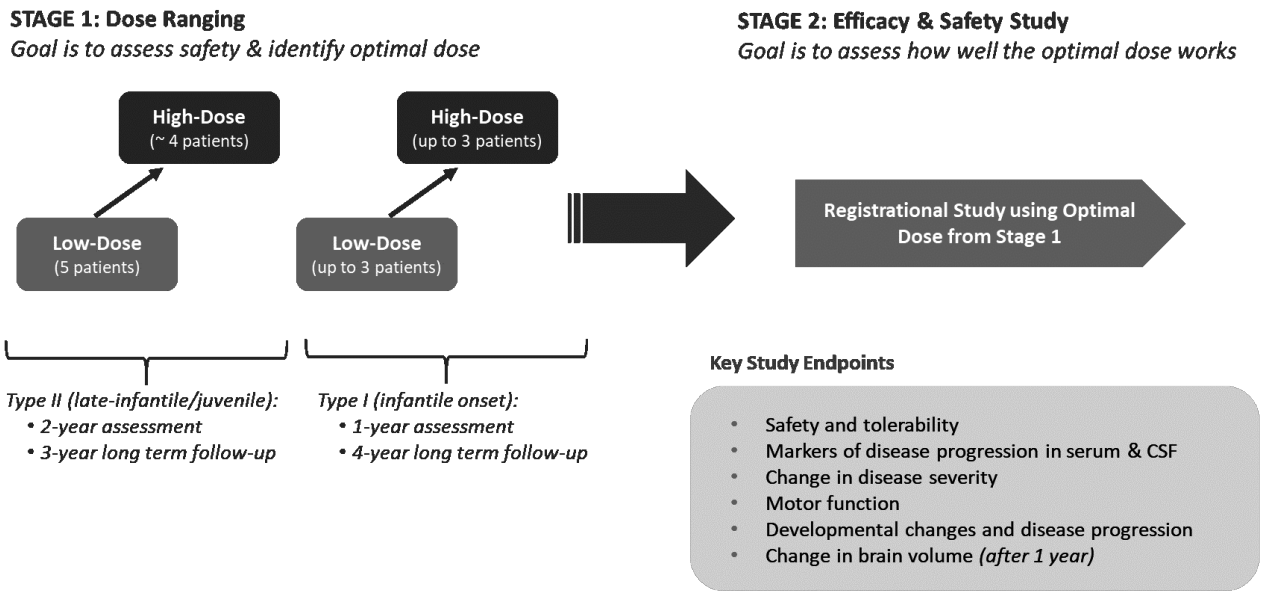
AXO-AAV-GM1 is currently being evaluated in an IND filed by the NIH. We presented an update from the first child dosed with AXO-AAV-GM1 in the fourth quarter of calendar year 2019, who was observed to have clinically significant improvements from baseline gene transfer to six month follow-up based on neurological exam, the Vineland-3 scale, Clinical Global Impression assessments, and nutritional status. The Vineland-3 scale is an individually administered measure of adaptive behavior that is widely used to assess individuals with intellectual, developmental, and other disabilities. In addition, AXO-AAV-GM1 was observed to be generally well tolerated with four treatment emergent adverse events, of which two were considered possibly related (increased Fibrin D dimer and increased aspartate aminotransferase ("AST"), both of which resolved with no clinical sequelae), and no reports of serious adverse events related to the investigational gene therapy or intravenous administration of the vector.

We have completed the enrollment and dosing of the five Type II (late-infantile/juvenile) patients in the low-dose cohort in Stage 1 of the registrational study of both Type I and Type II GM1 patients and announced initial data on the first cohort in December 2020. A total of five Type II patients were included in the initial data announced in December 2020. All patients had documented deficiency of β-gal enzyme activity with a genetic and clinical diagnosis of GM1 gangliosidosis. All five patients exhibited impairment of fine motor skills and change in walking pattern on clinical history at baseline. AXO-AAV-GM1 was generally well-tolerated at the low dose (1.5×10^{13} vg/kg) delivered intravenously, with no serious adverse events ("SAE" or "SAEs") reported as related to gene therapy. One SAE was described, whereby a single patient was diagnosed with bacterial sepsis resulting from an infection of the line used for drug product administration, which was considered to be unrelated to the investigational drug product, and which resolved within a few days following line removal and administration of antibiotics. The most common adverse events were considered mild to moderate. Transient and mild AST elevations were observed in four subjects, none of which required clinical intervention or had associated clinical consequences. There were no other adverse events indicative of impaired liver function. No clinically relevant changes were observed in platelet count.

We believe the favorable tolerability in the low-dose cohort supports continued enrollment of patients in the high-dose cohort (4.5×10^{13} vg/kg), in which two Type II patients have now been dosed without complications. At month six, serum enzyme activity increased by an average of 71% from baseline (range: 33%-127%) across the five patients in the first cohort. On average, serum β-gal enzyme activity was restored to 38% of normal reference levels at month six, with individual patients ranging from 23-57% of normal reference levels. The reference level was defined by the lowest level of enzyme activity in serum from 30 healthy adult volunteers using the same validated assay of β-gal enzyme activity as was used to assess the patients in the study. Cerebrospinal fluid ("CSF") samples were collected from all patients through lumbar puncture. Development and validation of biomarker assays for CSF β-gal enzyme is currently ongoing.

Patients were assessed by multiple measures of neurodevelopment including (i) the Vineland Adaptive Behavior Scales 3rd Edition ("VABS-3"), (ii) upright and floor mobility score, and (iii) Clinical Global Impression ("CGI"), a clinician's assessment of change in disease severity from baseline. VABS-3 is a standardized measure of adaptive behavior that is widely used to evaluate communication, daily living, social skills, and motor function. VABS-3 scores have a predictable relationship to ability, allowing for comparative assessments with increasing age. In GM1 gangliosidosis, predictable functional decline in abilities has been well documented in natural history studies, showing an age-related statistically significant decline in all sub-domains of the VABS-3 scale and in floor and upright mobility scores compared with unaffected children. All five patients demonstrated disease stability at six months post-treatment as assessed by VABS-3 growth scale value scores, upright and floor mobility score, and CGI relative to baseline values. Subdomain growth scale value scores in the VABS-3 remained stable or improved in four out of five patients. In May 2021, we presented new biomarker data at the American Society of Gene and Cell Therapy (ASGCT) conference demonstrating that, in addition to the six-month clinical data previously reported, the accumulated substrate GM1 ganglioside in the CSF was reduced from baseline by 18% to 49% in four out of five patients in the low-dose cohort. One patient, whose disease was the most advanced at baseline and who worsened on certain clinical parameters, exhibited an increase in CSF GM1 ganglioside of 19% from baseline at six months. Management believes these data represent the first direct evidence that intravenously administered AXO-AAV-GM1 exerts a measurable biochemical effect on reducing the toxic GM1 ganglioside that has accumulated in the CNS. Additional data will be collected at the 12-month evaluation including several measures of the systemic manifestations of GM1 gangliosidosis. We expect 12-month followup data on the first cohort to be available during the second half of calendar year 2021. In calendar year 2021, we plan to complete dosing in the high-dose cohort of Type II patients and the low-dose cohort of Type I patients in Stage 1 of the AXO-AAV-GM1 clinical program. In October 2020, the FDA granted Rare Pediatric Disease designation to AXO-AAV-GM1.

Our planned Stage 1 dose ranging study activities, Stage 2 efficacy and safety study activities and key study endpoints for our AXO-AAV-GM1 clinical program are summarized as follows:



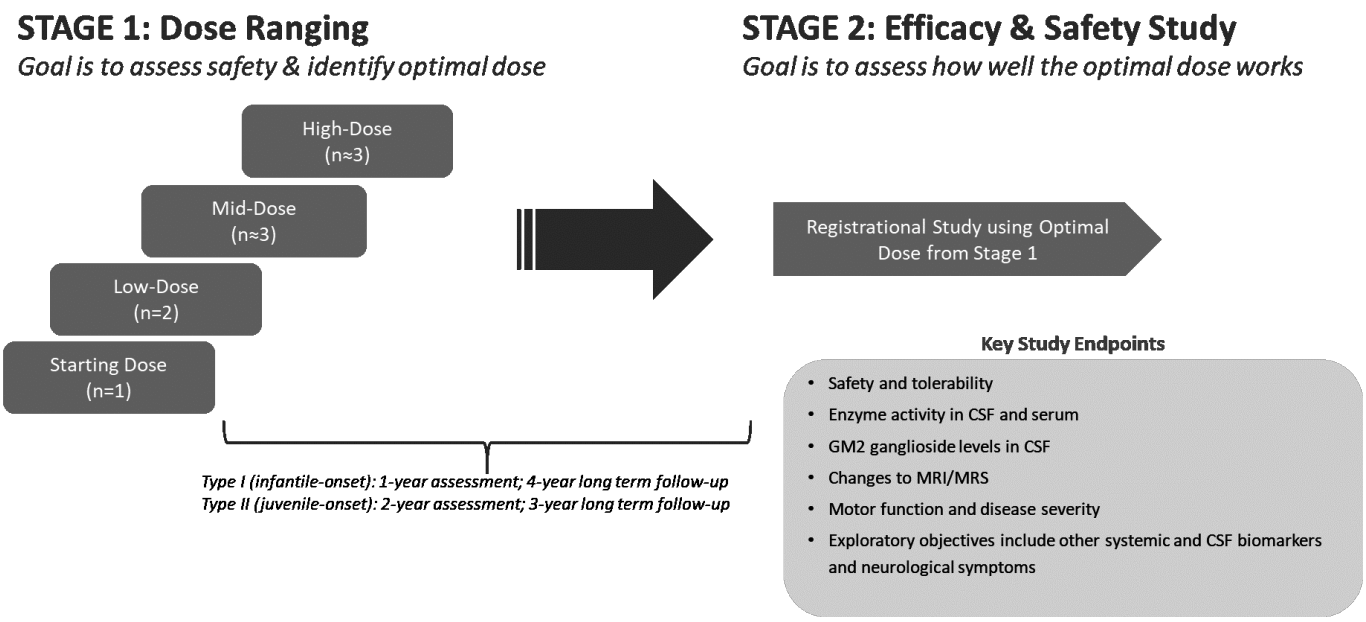
AXO-AAV-GM2

AXO-AAV-GM2 is an investigational gene therapy that we are developing as a potential one-time disease modifying treatment for GM2 gangliosidosis (including Tay-Sachs disease and Sandhoff disease). The AXO-AAV-GM2 program utilizes dual AAV vectors to deliver functional copies of both the *HEXA* gene and the *HEXB* gene, with the goal of restoring normal Hex A enzyme function in the CNS. AXO-AAV-GM2 is administered directly to the brain and CNS and utilizes the neurotropic AAVrh.8 capsid. The *HEXA* and *HEXB* genes will be delivered in a 1:1 ratio using separate AAvrh.8 vectors. As part of the AXO-AAV-GM2 program, we are also exploring a next-generation gene therapy that would utilize a bicistronic vector to deliver both the *HEXA* and *HEXB* genes in a single vector using the AAV9 capsid for systemic intravenous administration. We licensed exclusive worldwide rights for the development and commercialization of AXO-AAV-GM2 from UMMS in December 2018.

Administration of AXO-AAV-GM2 in the Sandhoff mouse model showed increases in Hex A enzyme, reductions of GM2 ganglioside in the brain, and improvements in motor coordination. Extension of survival was also observed in the Sandhoff mouse model, with increases in survival in a dose-dependent manner. Patients with infantile Tay-Sachs disease, late-infantile or juvenile disease, and adult disease have been shown to have less than 0.1%, approximately 0.5%, and between 2% and 4% of normal Hex A activity, respectively. In addition, patients with infantile Tay-Sachs disease, late-infantile or juvenile disease, and adult disease have a median survival time from birth of three to four, 10 to 15, and over 18 years, respectively. Hex A activity of between 5% and 10% or more of normal is believed to be compatible with a disease-free life. We believe that the restoration of Hex A activity to 0.5% of normal activity could represent a clinically meaningful effect.

In October 2020, the FDA granted Rare Pediatric Disease Designation to AXO-AAV-GM2. In November 2020, the FDA cleared an IND to support the initiation of our registrational clinical trial in patients with GM2 gangliosidosis. We have dosed the first infantile patient in the clinical trial under this IND in January 2021. The patient received 1.42×10^{14} vg divided into bilateral intra-thalamic and intra-thecal dosing.

Our planned Stage 1 dose ranging study activities, Stage 2 efficacy and safety study activities and key study endpoints for our AXO-AAV-GM2 clinical program are summarized as follows:



AXO-Lenti-PD Program

Overview

AXO-Lenti-PD is an *in vivo* lentiviral gene therapy investigational product candidate currently being developed as a potential one-time treatment of Parkinson's disease. We licensed the worldwide development and commercialization rights to AXO-Lenti-PD and ProSavin from Oxford Biomedica (UK) Ltd. ("Oxford"), under an exclusive license agreement entered into in June 2018 (the "Oxford Agreement"). Currently, we have six years of data on 15 patients dosed in a Phase 1/2 clinical trial of ProSavin and 24-month data on two patients dosed in Cohort 1 of the Phase 2 clinical trial of the SUNRISE-PD study. We reported six-month data from the four patients dosed in Cohort 2 of the SUNRISE-PD study in October 2020.

AXO-Lenti-PD delivers a construct of three genes that encode the critical enzymes required for the biochemical synthesis of dopamine from endogenous tyrosine. The three enzymes are: Tyrosine Hydroxylase ("TH"), the enzyme that converts tyrosine to levodopa ("L-dopa"), Cyclohydrolase 1 ("CH1"), the rate-limiting enzyme for synthesis of Tetrahydrobiopterin ("BH4"), a critical cofactor for production of L-dopa, and Aromatic L-Amino Acid Decarboxylase ("AADC"), the enzyme that converts L-dopa to dopamine. AXO-Lenti-PD is delivered by a one-time stereotactic guided infusion into the putamen. We believe that delivery of all three of these genes will enable the continuous, tonic, endogenous synthesis of dopamine in this region of the brain that is deficient in dopamine, with a goal of improving motor function, reducing the burden of oral therapy and mitigating dyskinesia in patients with Parkinson's disease.

Dopamine deficiency plays a central role in Parkinson's disease and we believe that restoring the ability to synthesize dopamine in patients will offer lasting improvement in the symptoms of Parkinson's disease. Oxford previously conducted a Phase 1/2 clinical study with ProSavin. In this clinical trial, ProSavin was observed to have a favorable long-term safety profile and demonstrated effects on motor function for six years, supporting proof-of-concept. AXO-Lenti-PD delivers a re-engineered construct relative to ProSavin that has been demonstrated to increase dopamine production in nonclinical studies.

Parkinson's Disease

Parkinson's disease is a chronic neurodegenerative disorder that primarily results in progressive and debilitating motor symptoms. It is estimated that up to 1,000,000 people in the United States and 7,000,000 to 10,000,000 people worldwide suffer from Parkinson's disease. It typically develops between the ages of 55 and 65 years and affects approximately 1% of people 60 years of age. The underlying factors that result in the development of Parkinson's disease are largely unknown. However, Parkinson's disease is a neurodegenerative disease that results in reduced levels of the neurotransmitter dopamine in the striatum, a region in the brain responsible for motor control. Dopamine is essential for movement, and low levels of dopamine in patients with Parkinson's disease are believed to result in the typical motor symptoms of the disease, including hypo- and bradykinesia, rigidity, tremor, and postural instability.

The treatment of Parkinson's disease is currently limited to symptomatic treatments, as no therapies have proven effective in altering the course of the disease or addressing the underlying pathophysiological processes. The mainstay of treatment typically involves the daily administration of oral L-dopa, the precursor to dopamine. While L-dopa is effective in controlling motor symptoms early in the disease, progressive loss of dopaminergic neurons and chronic L-dopa therapy are believed to contribute to the "*wearing off*" of L-dopa's efficacy in the more advanced stages of the disease. Patients become increasingly less responsive to oral L-dopa therapy and require higher doses to manage their symptoms. More advanced Parkinson's disease patients often begin to experience "*on-off*" motor fluctuations, characterized by unpredictable "OFF periods" of reduced mobility and increased rigidity and tremor. In addition, abnormal and involuntary movements known as dyskinesias may occur at higher L-dopa blood levels. Approximately 10% of patients per year develop "*on-off*" motor fluctuations after starting L-dopa therapy.

As Parkinson's disease progresses, other therapies can be used in combination with L-dopa and include dopamine receptor agonists and inhibitors of enzymes related to dopamine metabolism, such as monoamine oxidase B ("MAO-B") and catechol O-methyl transferase ("COMT"). These therapies aim to further improve overall dopaminergic function. Patient-friendly treatment options for motor fluctuations in advanced Parkinson's disease are limited. Subcutaneous injections of the dopamine agonist apomorphine are used for the acute treatment of OFF periods. Duopa/Duodopa is an enteral suspension of L-dopa and the peripheral AADC inhibitor carbidopa that is continuously administered over the course of the day through a surgically-placed percutaneous endoscopic gastrostomy with jejunal ("PEG-J") tube to reduce fluctuations in L-dopa blood levels. Deep-Brain Stimulation ("DBS"), a procedure in which electrodes are surgically placed in the basal ganglia, either in the subthalamic nucleus or internal globus pallidus, is another option for advanced Parkinson's disease. Through an impulse generator, electrical stimuli are delivered to the brain to modulate neural signals within these target regions. It remains unclear exactly how DBS improves the symptoms of Parkinson's disease. Both Duopa/Duodopa and DBS require indwelling hardware - a PEG-J tube, or electrodes, leads, and impulse generator - respectively.

Earlier-Generation Product Candidate: ProSavin (OXB-101)

ProSavin, the earlier-generation gene therapy candidate to AXO-Lenti-PD, delivered the same three genes (AADC, TH, and CH1) as AXO-Lenti-PD in the same lentiviral vector with a different payload configuration that demonstrated less activity. AXO-Lenti-PD was the result of multifactorial experimentation to optimize the payload configuration to increase endogenous dopamine production over that produced by ProSavin. The initial Phase 1/2 clinical trial of ProSavin was completed in 2012 and long-term follow-up is ongoing.

Nonclinical Studies for ProSavin

In nonclinical studies in non-human primate models of Parkinson's disease, ProSavin was shown to be well-tolerated, restored striatal dopamine production to approximately 50% of normal levels and improved motor function without associated dyskinesias (p-value<0.05). ProSavin was observed to improve Parkinson's disease symptoms and clinical disease severity in the same non-human primate model, with a durable response seen up to 12 months (p-value<0.05 at all time points beyond week 4). One of the ProSavin treated non-human primates was continued on the study and exhibited a sustained motor improvement until the study was concluded at 44 months. Also, in non-human primate models, treatment with ProSavin plus oral levodopa significantly reduced dyskinesias ($p<0.05$) compared to an empty vector plus oral levodopa, with effects sustained out to eight weeks. Nonclinical study data did not reveal adverse reactions nor findings with potential impact on patient safety and provided pertinent data on the optimal method of delivery in the clinic. ProSavin was also observed to be well tolerated when co-administered with L-dopa and apomorphine, indicating that it may possibly be used in conjunction with these commonly prescribed Parkinson's disease medications.

In summary, these experiments were determined to demonstrate the long-term safety of therapeutic doses of ProSavin as well as significant efficacy to improve measures of movement and reduce dyskinesias in animal models. These results supported the initiation of clinical trials for ProSavin.

Phase 1/2 Clinical Trial of ProSavin

ProSavin was evaluated for safety and efficacy in a Phase 1/2 study in patients with advanced Parkinson's disease by Oxford. In this study, ProSavin was observed to be well-tolerated with sustained improvements on motor function as measured by the UPDRS Part III (motor) score in the state "OFF" levodopa medication, which we refer to as UPDRS Part III "OFF." The Phase 1/2 clinical trial was conducted at sites in the United Kingdom ("U.K.") and France on a total of 15 patients with advanced Parkinson's disease. Three target dose levels of ProSavin were assessed in four patient cohorts: Low Dose: 1.9×10^7 transducing units ("TU") in Cohort 1 (n=3); Mid Dose: 4.0×10^7 TU in Cohorts 2a (n=3) and 2b (n=3); High Dose: 1.0×10^8 TU in Cohort 3 (n=6). Cohorts 2b and 3 underwent a modified delivery method to increase the rate of delivery of the viral vector. The primary endpoints were the number and severity of adverse events as well as the UPDRS Part III "OFF" scores at six months after gene therapy administration. No serious adverse events related to ProSavin or the surgical procedure were reported. Reported treatment emergent adverse events were generally mild and related to either Parkinson's disease progression or L-dopa-induced dyskinesias that were ameliorated with reduction of L-dopa administration. The most common adverse events in the first 12 months were dyskinesia (n=11 subjects), "*on-off*" motor fluctuations (n=9), headache (n=4), and akinesia (n=3).

Across all patients, mean UPDRS Part III "OFF" scores were significantly improved at six months (33% reduction, p-value=0.0001) and 12 months (31% reduction, p-value=0.0001) compared to baseline. In a long term follow up safety study for the patients from the Phase 1/2 study, ProSavin has been observed to show a favorable long-term safety profile and demonstrated positive effects on motor function for over six years. Sustained improvement was seen through six years of follow-up and the long-term follow-up study is still ongoing (10 years exposure in the earliest subject). Clinical data from this study were published in The Lancet in 2014 and long-term follow-up data from this study were published in Human Gene Therapy Clinical Development in 2018.

Next-Generation Product Candidate: AXO-Lenti-PD

AXO-Lenti-PD is a re-engineered gene therapy product candidate that was selected following experimentation to optimize the payload configuration of ProSavin to increase endogenous dopamine production. The modifications included a different ordering of the genes, the fusion of TH and CH1 with a flexible linker, and the removal of a genetic control element between TH and AADC. Both ProSavin and AXO-Lenti-PD utilize the same exact fourth generation lentiviral vector. We believe these changes lead to more balanced stoichiometry of gene expression and colocalization of enzymatic activity. The targeted net result is increased dopamine production in transduced cells.

Nonclinical Studies for AXO-Lenti-PD

In vitro experiments in a human neuron model with AXO-Lenti-PD showed up to 10-fold increases in dopamine + L-dopa production over ProSavin. *In vivo* experiments in non-human primate models showed increased AADC activity in the brain with AXO-Lenti-PD compared to ProSavin as measured by positron emission tomography ("PET") scans. Functionally, in non-human primate models at approximately 1/5th of the dose, AXO-Lenti-PD demonstrated a similar level of improvement in spontaneous locomotor activity compared to ProSavin. A recent placebo-controlled study in a non-human primate model of Parkinson’s disease published in *Molecular Therapy: Methods and Clinical Development* compared two doses of AXO-Lenti-PD against control-group animals receiving a placebo. The study demonstrated statistically significant differences in Parkinson's disease clinical response scores at six months in this diseased-animal model ($p<0.0002$ for AXO-Lenti-PD compared to control), dose-dependent increases in PET signaling using a 6-[(18)F]fluoro-m-tyrosine radiotracer ($p<0.001$ for AXO-Lenti-PD compared to control), and dose-dependent increases in gene expression for AADC, TH, and CH1 in transduced striatal tissue. We believe these data provide evidence that AXO-Lenti-PD may have greater potency compared to ProSavin in terms of dopamine production, enzymatic activity and functional improvement in animal models of Parkinson's disease.

In May 2021, we presented data from a non-human primate study of AXO-Lenti-PD designed to evaluate the impact of (i) changes to suspension-based manufacturing process material, (ii) increased volume and flow rate during simultaneous bilateral infusions, and (iii) use of a new stereotactic frame. This study found no evidence for neuropathology changes associated with the new administration procedure. Biodistribution was limited to the area of infusion with no expression detected in distal brain regions or peripheral organs or shedding matrices. Furthermore, no differences in immunological profile were observed using the early-stage suspension process-produced AXO-Lenti-PD material versus adherent process-produced material. These toxicology results support the planned clinical development plan for ongoing dose, procedure, and administration systems evaluations.

SUNRISE-PD Phase 2 Clinical Trial of AXO-Lenti-PD

In the fourth quarter of calendar year 2018, we initiated the Phase 2 clinical trial of the SUNRISE-PD study in the U.K. The SUNRISE-PD study is currently enrolling patients in the U.K., and we plan to file an investigational medicinal product dossier application to support the enrollment of additional patients using the suspension-based manufacturing process. Additionally, we have filed a Clinical Trial Application to support local enrollment in France.

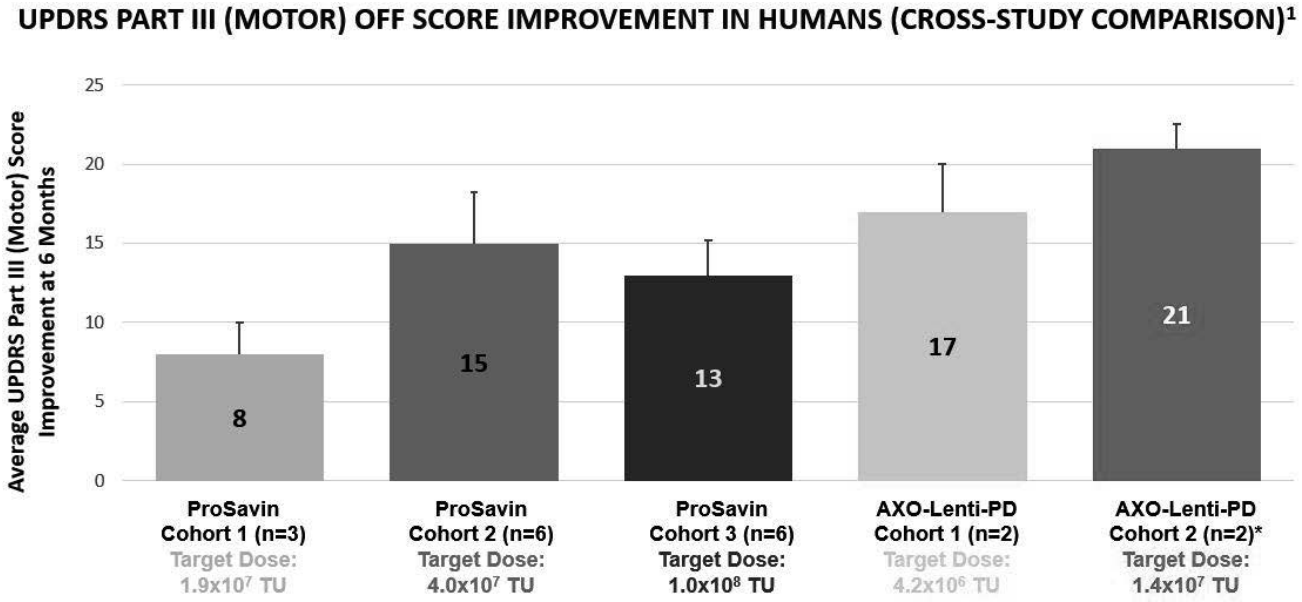
The design of the SUNRISE-PD study is an open label dose-escalation portion studying multiple dose levels. Once the optimal dose has been determined in the dose-escalation study, a sham-controlled study will be conducted with patients randomized either to an active group receiving the optimal dose as determined in the SUNRISE-PD study, or a control group undergoing an imitation "sham" surgical procedure. We are working closely with our manufacturing partner for AXO-Lenti-PD, Oxford Biomedica, to develop a reliable suspension-based manufacturing process. Manufacturing of several GMP batches using a revised suspension-based process has been ongoing at Oxford Biomedica with a goal of generating material for use in future clinical trials. We expect a batch to be released that can be used for dosing of further patients in the SUNRISE-PD study in the fourth calendar quarter of 2021, pending an updated filing with the Medicines and Healthcare products Regulatory Agency (the "MHRA") in the UK. Once the MHRA accepts the filing, we plan on dosing two additional patients at the mid-dose (1.4×10^7 TU) to evaluate a revised surgical procedure before proceeding to dosing patients at the next higher dose (4.2×10^7 TU).

The sham-controlled study will evaluate the safety and tolerability of AXO-Lenti-PD as well as assessing efficacy using clinical measures of motor function, patient diaries and biomarkers. We expect the primary endpoint of the double-blind, randomized, sham-controlled study to be assessed at a regulatory appropriate timepoint and, in addition to the safety assessment, efficacy evaluations may include data from Hauser patient diaries, the UPDRS Part III and Part II "OFF" scores and other efficacy measures being assessed in the study.

In January 2020, we reported 12-month data from Cohort 1 in the open-label, dose-escalation SUNRISE-PD Phase 2 study. AXO-Lenti-PD was observed to be generally well tolerated, with no serious adverse events attributable to the gene therapy. At month 12, the patients experienced an average improvement from baseline in UPDRS III (motor) score, in the state "OFF" levodopa therapy, of 22 points, representing an average improvement of 37% from baseline. Individual patient improvements from baseline at 12 months of 20 points and 24 points were observed (from 58 to 38 and from 60 to 36, respectively). Previously, at six months post-dosing, these patients demonstrated an average 17-point change from baseline, or 29% improvement, on the same scale. Only one of two patients in Cohort 1 was able to record a Hauser diary. Improvements were observed across various diary measures from baseline to 12 months for the single patient. The Parkinson's Disease Questionnaire-39 score index, a well-validated quality of life measure in Parkinson’s disease, demonstrated an average 15-point change from baseline for the patients in Cohort 1, or 30% improvement from baseline to 12 months. In addition, the patients experienced an average improvement of approximately 13 points from baseline on the UPDRS Part II (activities of daily living) "OFF" score at 12 months post-dosing, representing an average improvement of 44% from baseline, and an average improvement of 3 points from baseline on the UPDRS Part IV (complications of therapy) "OFF" score at six months post-dosing. The 12-month timepoint is considered an important timeframe for assessment of therapeutic response, differentiation from sham/placebo effect, and durability of gene therapy in Parkinson’s disease.

We dosed the first patient in Cohort 2 of the SUNRISE-PD clinical study in April 2019 and the last (fourth) patient in February 2020. The target dose being tested in Cohort 2 is 1.4×10^7 TU, which is three times higher than the dose used in Cohort 1. In October 2020, we reported that all of the four patients in the cohort were able to complete the evaluations that do not require an inpatient visit (Hauser diary, Levodopa Equivalent Daily Dose), and only two of the four were able to complete the UPDRS Part II and III evaluations – one patient refused this evaluation and the other was not able to be seen in the clinic since it was closed due to COVID-19 response measures. AXO-Lenti-PD was observed to be generally well tolerated, with no serious adverse events attributable to the gene therapy. At month 6, the patients experienced an average improvement from baseline in UPDRS Part III (motor) score, in the state "OFF" levodopa therapy, of 21 points, representing an average improvement of 40% from baseline. Individual patient improvements from baseline at 6 months of 22 and 19 points were observed. Similarly, at six months, the patients experienced an improvement in the UPDRS Part II (quality of life) of 14 points, which represents a 71% improvement. Individual patients’ improvement from baseline were 12 and 15 points. The Hauser diary was completed by all four patients and demonstrated an improvement from baseline of 2.3 hours in OFF time and 2.2 hours in good ON time.

Improvement in the UPDRS Part III “OFF” score in Cohort 1 and Cohort 2 exhibited evidence of dose response when compared to the low (n="3"), medium (n="6"), and high (n="6") dose cohorts of ProSavin that were previously evaluated in a separate Phase 1/2 study at six months, as follows:



[1]Palfi, et al. The Lancet. 2014;383(9923):1138-1146. Note: Error bars are calculated as (Mean +/- SEM)

*UPDRS data is only available for two patients at six months post-dosing.

Our Key Agreements

The University of Massachusetts Medical School Exclusive License Agreement

In December 2018, we entered into an exclusive license agreement (the "UMMS Agreement") with UMMS pursuant to which we received a worldwide, royalty-bearing, sub-licensable license under certain patent applications and any patents issuing therefrom, biological materials and know-how controlled by UMMS to develop and commercialize gene therapy product candidates, including AXO-AAV-GM1 and AXO-AAV-GM2, for the treatment of GM1 gangliosidosis and GM2 gangliosidosis (including Tay-Sachs disease and Sandhoff disease). This license is exclusive with respect to patents and biological materials and non-exclusive with respect to know-how and is subject to UMMS' retained rights for academic research, teaching and non-commercial patient care purposes, as well as to certain pre-existing rights of the U.S. government.

Under the UMMS Agreement, we are solely responsible, at our expense, for the research, development and commercialization of the licensed product candidates. We will reimburse UMMS for payments made by UMMS for the manufacture of clinical trial materials for us, up to a specified amount. UMMS is a clinical trial site for our AXO-AAV-GM2 program. We are obligated to use diligent efforts to develop and commercialize the licensed product candidates and are required to achieve certain development and commercial milestones in accordance with the timeline set forth in the agreement.

Under the terms of the UMMS Agreement, we made an upfront payment of $10.0 million. In addition, we could be obligated to make payments to UMMS totaling up to $24.5 million upon the achievement of specified development and regulatory milestones and $39.8 million upon the achievement of specified commercial milestones. In February 2019, certain development and regulatory milestones were achieved resulting in a $1.0 million payment to UMMS, and in October 2019, further development and regulatory milestones were achieved resulting in an additional $1.0 million payment due to UMMS. We are also obligated to pay UMMS tiered mid-single digit royalties based on yearly net sales of the licensed products, subject to a specified annual minimum amount. Additionally, we will pay UMMS a percentage of any revenues we receive from any third-party sublicenses to licensed products at rates ranging in the mid-single digits to mid-teens.

The UMMS Agreement expires upon the expiration of our obligations to make royalty payments to UMMS, which continues until the later of the expiration of licensed patents and any applicable orphan designation exclusivity and 10 years after the first commercial sale of the licensed products. Upon such expiration, the licenses granted to us by UMMS will automatically convert to perpetual, irrevocable, worldwide royalty-free licenses. We have the right to terminate the UMMS Agreement at any time upon 90 days' advance written notice to UMMS. Either party may terminate the UMMS Agreement for the other party's uncured material breach upon 60 days' advance written notice, including in the event that UMMS reasonably determines we have not fulfilled our diligence obligations.

Oxford Biomedica License Agreement

In June 2018, we entered into the Oxford Agreement, pursuant to which we received a worldwide, exclusive, royalty-bearing, sub-licensable license under certain patents and other intellectual property controlled by Oxford to develop and commercialize AXO-Lenti-PD and related gene therapy products for all diseases and conditions. In June 2018, as partial consideration for the license, we made an upfront payment to Oxford of $30.0 million, $5.0 million of which was applied as a credit against the process development work and clinical supply that Oxford is obligated to provide to us over the term of the Oxford Agreement. Under the terms of the Oxford Agreement, we could be obligated to make payments to Oxford totaling up to $55.0 million upon the achievement of specified development milestones and $757.5 million upon the achievement of specified regulatory and sales milestones. In April 2019, certain development milestones were achieved resulting in a $13.0 million net payment due to Oxford. We will also be obligated to pay Oxford a tiered royalty from 7% to 10%, based on yearly aggregate net sales of the underlying gene therapy products, subject to specified reductions upon the occurrence of certain events as set forth in the Oxford Agreement. These royalties are required to be paid, on a product-by-product and country-by-country basis, until the latest to occur of the expiration of the last to expire valid claim of a licensed patent covering such product in such country, the expiration of regulatory exclusivity for such product in such country, or 10 years after the first commercial sale of such product in such country.

We are solely responsible, at our expense, for all activities related to the development and commercialization of the gene therapy products. Pursuant to the Oxford Agreement, we are required to use commercially reasonable efforts to develop, obtain regulatory approval of, and commercialize a gene therapy product in the United States and at least one major market country in Europe. In addition, we are required to meet certain diligence milestones and to include at least one U.S.-based clinical trial site in a pivotal study of a gene therapy product. If we fail to meet any of these specified development milestones, we may cure such failure by paying Oxford certain fees, which range from $0.5 million to $1.0 million. In July 2020, we entered into a three-year clinical supply agreement with Oxford for the manufacturing and supply of cGMP batches to support the ongoing and future clinical development of AXO-Lenti-PD. If Oxford completes the development of a suspension-based manufacturing process, and successfully produces clinical supplies for our studies, we anticipate that future commercial supply for the AXO-Lenti-PD program will be manufactured by Oxford in accordance with a separate cGMP commercial supply agreement to be negotiated between the parties. We have the right to terminate the Oxford Agreement at any time upon two months' advance written notice prior to the first commercial sale of a product, or for a specified period of advance written notice after the first commercial sale of a product. Either party may terminate the Oxford Agreement for the other party's uncured material breach or with respect to a failure to make a required payment.

Manufacturing

We currently do not own or operate facilities for product manufacturing but work with third parties and our license partners to manufacture our program materials. We have hired experienced personnel and continue to build a team with gene therapy product formulation and manufacturing expertise.

For the AXO-Lenti-PD program, we rely on inventory transferred to us under the Oxford Agreement to support our ongoing Phase 2 study. In July 2020, we entered into a three-year clinical supply agreement with Oxford for the manufacturing and supply of cGMP batches to support the ongoing and future clinical development of AXO-Lenti-PD. We are working closely with our manufacturing partner for AXO-Lenti-PD, Oxford Biomedica, to develop a reliable suspension-based manufacturing process. Manufacturing of several GMP batches using a revised suspension-based process has been ongoing at Oxford Biomedica with a goal of generating material for use in future clinical trials. We expect a batch to be released in the fourth calendar quarter of 2021 that can be used for dosing of further patients in the SUNRISE-PD study, pending an updated filing with the MHRA in the UK.

If Oxford completes the development of a suspension-based manufacturing process, and successfully produces clinical supplies for our studies, we anticipate that future commercial supply for the AXO-Lenti-PD program will be manufactured by Oxford in accordance with a separate cGMP commercial supply agreement to be negotiated between the parties. As set forth in the Oxford Agreement, such clinical and commercial supply agreements will contain certain key provisions, including the pricing structure and our ability to transfer the technology to another manufacturer at any time following the completion of formal process characterization, process validation or BLA submission. We have the right to terminate the Oxford Agreement at any time upon two months' advance written notice prior to the first commercial sale of a product, or for a specified period of advance written notice after the first commercial sale of a product. Either party may terminate the Oxford Agreement for the other party's uncured material breach or with respect to a failure to make a required payment.

Manufacturing of any product candidate is subject to extensive regulations that impose various procedural and documentation requirements, which govern recordkeeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others.

Competition

We consider our direct competitors for AXO-AAV-GM1 or AXO-AAV-GM2 to be LYS-GM101, a gene therapy product candidate being developed by Lysogene S.A., as well as PBGM01, a gene therapy program being developed by Passage Bio which recently received IND clearance, each for the treatment of GM1 gangliosidosis, and TSHA-101, a gene therapy product candidate being developed by Taysha Gene Therapies for the treatment of GM2 gangliosidosis.

We consider our most direct competitor with respect to AXO-Lenti-PD to be Voyager Therapeutics, which was previously advancing VY-AADC, a gene therapy product candidate for the treatment of advanced Parkinson's disease. VY-AADC delivers the AADC gene, one of the three genes contained in AXO-Lenti-PD, via an adeno-associated virus (an "AAV virus-based vector"). In May 2021, Voyager Therapeutics announced that it will not advance the VY-AADC program on its own following the termination of that portion of the collaboration agreement with Neurocrine Biosciences. Agilis Biotherapeutics, which was acquired by PTC Therapeutics, is developing AGIL-AADC, another AAV virus-based vector gene therapy that delivers the AADC gene, for the treatment of AADC deficiency, a rare disorder that involves loss of AADC gene function. In addition, DBS is approved for treating Parkinson's disease and is marketed by multiple device manufacturers, including Medtronic, Abbott and Boston Scientific. DBS treatment involves permanent placement of hardware in the brain via stereotactic neurosurgery and may require follow-up adjustments or even invasive device replacements. Another surgical approach is Abbvie's Duopa which is delivered via a port implanted in the abdominal wall. Further efforts are also underway to develop and commercialize new improved formulations of L-dopa, including Acorda's Inbrija, for which an NDA was approved by the FDA in December 2018, and Mitsubishi Tanabe's ND0612. Adjunct therapies are also being developed or have recently been approved to supplement L-dopa therapy, including Sunovion's sublingual apomorphine and Adamas Pharmaceuticals' GoCovri. Several companies are also trying to develop other disease modifying therapies that could prevent the progression of Parkinson's disease. MeiraGTx is developing AAV-GAD, a gene therapy product designed to deliver the GAD gene to increase production of the neurotransmitter GABA to normalize motor circuits. Examples of early stage efforts include Denali Therapeutics' LRRK2 inhibitors and anti-alpha synuclein antibodies from Prothena/Roche and Biogen, as well as Prevail Therapeutics' (acquired by Eli Lilly in 2020) pipeline of AAV-based therapeutics targeting lysosomal dysfunction. BlueRock Therapeutics (acquired by Bayer in 2019) is developing an induced pluripotent stem cell-derived (iPSC) dopaminergic neuron therapy for patients with Parkinson's and will enter a Phase 1 clinical trial in 2021 to evaluate the safety, tolerability, and preliminary efficacy in patients with Parkinson's disease.

Drug development is highly competitive and subject to rapid and significant technological advancements. Our ability to compete will depend upon our ability to complete necessary clinical trials and regulatory approval processes, and effectively market any product that we may successfully develop. Our current and potential future competitors include pharmaceutical and biotechnology companies, academic institutions and government agencies. The primary competitive factors that will affect the commercial success of any product candidate for which we may receive marketing approval include efficacy, safety and tolerability profile, dosing convenience, price, coverage and reimbursement. Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, as well as in obtaining regulatory approvals of those product candidates in the United States and in foreign countries. Our current and potential future competitors also have significantly more experience commercializing drugs, particularly gene therapy and other biological products, that have been approved for marketing. Mergers and acquisitions in the pharmaceutical and biotechnology industries could result in even more resources being concentrated among a small number of our competitors.

Accordingly, our competitors may be more successful than us in obtaining regulatory approval for therapies and in achieving widespread market acceptance of their products. It is also possible that the development of a cure or more effective treatment method for Parkinson's disease, GM1 gangliosidosis and GM2 gangliosidosis (including Tay-Sachs and Sandhoff diseases) by a competitor could render our product candidates non-competitive or obsolete or reduce the demand for our product candidates before we can recover our development and commercialization expenses.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our current gene therapy product candidates, any of our future product candidates, novel discoveries, product development technologies and other know-how. Our commercial success also depends on our ability to operate without infringing on the proprietary rights of others and our ability to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patents and patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trademarks, trade secrets, copyrights, know-how, continuing technological innovation and potential in-licensing and acquisition opportunities to develop and maintain our proprietary position.

While we seek broad coverage under our existing patent applications, there is always a risk that an alteration to the process of obtaining patents or changes to the patent law in the United States or elsewhere may provide sufficient basis for a competitor to challenge or avoid infringement of our patents. In addition, patents, if granted, expire and we cannot provide any assurance that any patents will be issued from our pending applications or any future applications or that any future issued patents will adequately protect our intellectual property or cover our product candidates.

Individual patents are valid for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal patent term in the countries in which they are obtained. Generally, patents issued from regularly filed applications in the United States are granted a term of 20 years from the earliest non-provisional filing date. In addition, in certain instances, a patent's term can be extended via Patent Term Adjustment ("PTA") to recapture a portion of the U.S. Patent and Trademark Office's (the "USPTO") delay in issuing the patent as well as via Patent Term Extension ("PTE") to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the PTE period can be applied to only one patent per approved product, cannot be longer than five years and the total patent term including the PTE period must not exceed 14 years following FDA approval of an NDA or BLA. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest non-provisional filing date. The actual protection afforded by a patent varies on a product by product basis, on a claim by claim basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. The patent term of a European patent is 20 years from its filing date; however, unlike in the United States, a European patent is not granted PTA for delays at the European Patent Office. However, the European Union does have a compensation program similar to the U.S.'s PTE called Supplementary Patent Certificate ("SPC") that would effectively extend patent protection for term lost during regulatory delay, if any, for up to five years on one patent and the total patent term including the SPC must not exceed 15 years following the EMA granting of marketing authorization. Other major markets, including Japan, have similar patent term extension provisions and, if eligible, we intend to seek patent term extensions in those countries that have such programs.

In December 2018, we entered into the UMMS Agreement with UMMS. Pursuant to the UMMS Agreement, we received from UMMS a worldwide, royalty-bearing, sub-licensable license under certain patent applications and any patents issuing therefrom, and other intellectual property controlled by UMMS to develop and commercialize gene therapy product candidates, including AXO-AAV-GM1 for treatment of GM1 gangliosidosis and AXO-AAV-GM2 for treatment of GM2 gangliosidosis (including Tay-Sachs disease and Sandhoff disease). This license is exclusive with respect to patents and biological materials and non-exclusive with respect to know-how, and is subject to UMMS' retained rights for academic research, teaching and non-commercial patient care purposes, as well as to certain pre-existing rights of the U.S. government. The licensed IP includes pending U.S. and foreign patent applications directed to compositions of matter as well as methods of using AXO-AAV-GM1 and/or AXO-AAV-GM2 (separate or bicistronic vectors) in major markets, including the United States, the United Kingdom, Canada, Brazil, Korea, Japan, and China. These applications, if issued, include patent families that will expire starting in 2036, with the projected last to expire in 2039 (not taking into account any PTA or PTE, which may potentially be obtained in the future). Depending on certain factors, the term of a patent, if issued, covering an approved product may be extended by up to five years with PTE.

In June 2018, we entered into the Oxford Agreement with Oxford. Pursuant to the Oxford Agreement, we received from Oxford a worldwide, exclusive, royalty-bearing, sub-licensable license under certain patents and other intellectual property controlled by Oxford to develop and commercialize certain lentiviral-based gene therapy products for all diseases and conditions. Oxford is prohibited from granting licenses to third parties to develop, commercialize, or distribute such lentiviral-based gene therapy products. The licensed IP includes issued U.S. and foreign patents and pending U.S. and foreign patent applications that cover compositions of matter as well as methods of making and using AXO-Lenti-PD in major markets, including the United States, Japan, China, India, the United Kingdom, and Australia. These patents and applications, if issued, include patent families that expired starting at the end of 2018, with the projected last to expire in October of 2032 (not taking into account any PTA or PTE, which may potentially be obtained in the future). In addition, new patent application filings could provide patent coverage out to at least 2040, if a patent issues. U.S. composition of matter patents relevant to AXO-Lenti-PD will naturally expire in 2023 and 2035, each inclusive of PTA, and if further patents issue from the pending application families they will expire in 2032 or 2040 (not taking into account any PTA or PTE, which may potentially be obtained in the future). Depending on certain factors, the term of a patent covering an approved product may be extended by up to five years with PTE.

Furthermore, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part by using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements and invention assignment agreements with selected partners and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed by our employees or through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our product candidate(s) or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our gene therapy product candidate(s) may have an adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we believe we have rights, we may have to participate in interference or derivation proceedings in the USPTO to determine priority and/or inventorship of an invention.

Government Regulation

In the United States, pharmaceutical and biological products are subject to extensive regulation by the FDA under the Federal Food, Drug, and Cosmetic Act ("FDCA"), and the Public Health Service Act ("PHSA"). The FDCA, PHSA, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending BLAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

We cannot market a biological product, including gene therapy product candidates which are regulated as biologics, in the United States until the product candidate has received FDA approval. The steps required before a new biologic may be marketed in the United States generally include the following:

- completion of extensive nonclinical laboratory tests, animal studies, and formulation studies in accordance with the FDA's Good Laboratory Practice ("GLP") regulations;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice ("GCP") requirements to establish the safety and efficacy of the product for each proposed indication;
- submission to the FDA of a BLA, in the case of biological product candidates including gene therapy product candidates, after completion of all pivotal clinical trials;
- satisfactory completion of an FDA inspection of sites involved in our clinical trials;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the active pharmaceutical ingredient ("API") and finished product are produced and tested to assess compliance with cGMPs; and
- FDA review and approval of the BLA prior to any commercial marketing or sale of the product in the United States.

Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Nonclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the nonclinical tests must comply with federal regulations and requirements, including GLP regulations. The results of nonclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls and a proposed clinical trial protocol. Long-term nonclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. If the FDA raises concerns or questions about the conduct of the trial, such as whether human research subjects will be exposed to an unreasonable health risk, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed.

Clinical trials involve the administration of the investigational new biologic to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations, including GCP requirements, as well as under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board ("IRB") for approval at each site at which the clinical trial will be conducted. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

U.S. Biological Products Development Process

Before testing any biological product candidate, including a gene therapy product, in humans, the product candidate enters the nonclinical testing stage. Nonclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the nonclinical tests must comply with federal regulations and requirements including GLPs.

Where a gene therapy study is conducted at, or sponsored by, institutions receiving funding from the NIH for recombinant DNA research, the NIH Guidelines for Research Involving Recombinant DNA Molecules ("NIH Guidelines") are mandatory, however many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. An institutional biosafety committee ("IBC"), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution, assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. Annual reporting of clinical trial data including safety information also is required.

The clinical study sponsor must submit the results of the nonclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some nonclinical testing typically continues after the IND is submitted. An IND is an exemption from the FDCA that allows an unapproved product to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational product to humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA requests certain changes to a protocol before the study can begin, or the FDA places the clinical study on a clinical hold within that 30-day time period. 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, studies may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such studies.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or subjects 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 study, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical study 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 study must be reviewed and approved by an independent IRB, at or servicing each institution at which the clinical study 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 study subject or his or her legal representative and must monitor the clinical study until completed. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. Additionally, gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH also are potentially subject to review by a committee within the NIH's Office of Science Policy called the Novel and Exceptional Technology and Research Advisory Committee, or the NExTRAC. This review group focuses on clinical trials that cannot be evaluated by standard oversight bodies and pose unusual risks. With certain gene therapy protocols, FDA review of or clearance to allow the IND to proceed could be delayed if the NExTRAC decides that full public review of the protocol is warranted.

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

- Phase 1. The biological product 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. Guidelines on clinical trials with gene therapy products issued by the FDA's Office of Tissues and Advanced Therapies state that the FDA has determined that the benefit-risk ratio of these products does not warrant their evaluation in healthy human subjects.

- Phase 2. The biological product 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.

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, of trial subjects.

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 and the investigators for serious and unexpected adverse events, any findings from other studies, 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 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. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

Human gene therapy products are a new category of therapeutics, regulated as biologics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the study period, the number of patients the FDA will require to be enrolled in the studies in order to establish the safety, efficacy, purity and potency of human gene therapy products, or that the data generated in these studies will be acceptable to the FDA to support marketing approval.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHSA emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

After the completion of clinical trials of a biological product, FDA approval of a BLA, must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act ("PREA"), a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act, as amended ("PDUFA"), each BLA must be accompanied by a significant user fee. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for product candidates designated as orphan drugs, unless the product candidate also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. The application also needs to be published and submitted in an electronic format that can be processed through the FDA's electronic systems. If the electronic submission is not compatible with FDA's systems, the BLA can be refused to file. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe, potent, and effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP 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 ("REMS"), is necessary to assure the safe use of the biological product. 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 trial sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. To assure cGMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized. As a condition for approval, the FDA may also require additional nonclinical testing as a Phase 4 commitment.

One of the performance goals agreed to by the FDA under the PDUFA is to review standard BLAs in 10 months from filing and priority BLAs in six months from filing, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Maintaining substantial compliance with applicable federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Following approval, the manufacturing facilities are subject to biennial inspections by the FDA's biologics team and such inspections may result in an issuance of FDA Form 483 deficiency observations or a warning letter, which can lead to plant shutdown and other more serious penalties and fines. Prior to the institution of any manufacturing changes, a determination needs to be made whether FDA approval is required in advance. If not done in accordance with FDA expectations, the FDA may restrict supply and may take further action. Annual product reports are required to be submitted annually. 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. Systems need to be put in place to record and evaluate adverse events reported by health care providers and patients and to assess product complaints. An increase in severity or new adverse events can result in labeling changes or product recall. Defects in manufacturing of commercial products can result in product recalls.

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. 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 or license revocation, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs 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.

Market and Data Exclusivity

The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the Affordable Care Act, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidance is expected to be finalized by FDA in the near term.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the FDA must find that the biosimilar product can be expected to produce the same clinical results as the reference product and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. The BPCIA also requires a 180-day notice of commercial marketing. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own nonclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

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

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

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

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

EU Data and Marketing Exclusivity

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

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

EU Orphan Medicinal Products

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

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

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

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply enough orphan medicinal product.

EU Pediatric Investigation Plan

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

EU Post-Approval Controls

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

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

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

EU Pricing and Reimbursement

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

Other Healthcare Laws

Although we currently do not have any products on the market, our current and future business operations may be subject to additional healthcare regulation and enforcement by the U.S. federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, price reporting and physician sunshine laws. Some of our pre-commercial activities are subject to some of these laws.

The federal Anti-Kickback Statute makes it illegal for any person or entity, including a prescription drug manufacturer or a party acting on its behalf, to knowingly and willfully solicit, receive, offer, or pay any remuneration, directly or indirectly, that is intended to induce the referral of business, including the purchase, order, lease of any good, facility, item or service for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term "remuneration" has been broadly interpreted to include anything of value, including cash, improper discounts, and free or reduced-price items and services. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, formulary managers, and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the Anti-Kickback Statute has been violated.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Affordable Care Act, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

The federal false claims laws, including the civil False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, for payment to, or approval by, federal programs, including Medicare and Medicaid, claims for items or services, including drugs, that are false or fraudulent or not provided as claimed. Persons and entities can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, certain of our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law.

The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created additional federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal Anti-Kickback Statute, the Affordable Care Act amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH") and their implementing regulations, including the final omnibus rule published on January 25, 2013, mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, defined as independent contractors or agents of covered entities that create, receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity. At present, it is unclear if we would be considered a business associate subject to HIPAA based on our business activities and service offerings upon the commercialization of a product. HITECH also increased the civil and criminal penalties that may be imposed against covered entities and business associates and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, certain state and foreign laws, regulations, standards and regulatory guidance 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.

The Affordable Care Act, through the enactment of the Physician Payments Sunshine Act, imposes, among other things, new annual reporting requirements for covered manufacturers for certain payments and other transfers of value provided to physicians, as defined by such law, and teaching hospitals, as well as certain ownership and investment interests held by physicians and their immediate family members.

Many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. We may also be subject to state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, state laws that require drug manufacturers to report information related to pricing, payments and other transfers of value to physicians and other healthcare providers or marketing expenditures as well as state and local laws that require the registration of pharmaceutical sales representatives. Additionally, to the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws.

Because we intend to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs, we will continue to develop a comprehensive compliance program that establishes internal controls to facilitate adherence to the rules and program requirements to which we will or may become subject. Although the development and implementation of compliance programs designed to establish internal control and facilitate compliance can mitigate the risk of violating these laws, and the subsequent investigation, prosecution, and penalties assessed for violations of these laws, the risks cannot be entirely eliminated.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Foreign Corrupt Practices Act

We are subject to the Foreign Corrupt Practices Act of 1977, as amended ("FCPA"). The FCPA prohibits U.S. companies and their representatives from processing, offering, or making payments of money or anything of value to foreign officials with the intent to obtain or retain business or seek a business advantage. In certain countries, the health care professionals we regularly interact with may meet the definition of a foreign government official for the purposes of the FCPA. Our international activities create the risk of unauthorized payments or offers of payments by our employees, consultants and agents, even though they may not always be subject to our control. We discourage these practices by our employees, consultants, and agents. However, our existing safeguards may prove to be less than effective, and our employees, consultants, and agents may engage in conduct for which we might be held responsible. Recently, there has been a substantial increase in anti-bribery law enforcement activity by U.S. regulators, with more frequent and aggressive investigations and enforcement activity by both the Department of Justice and the SEC. A determination that our operations or activities are not, or were not, in compliance with U.S. or foreign laws or regulations could result in the imposition of substantial fines, interruptions of business, loss of suppliers, vendor or other third-party relationships, termination of necessary licenses or permits, and legal or equitable sanctions. Other internal or governmental investigations or legal or regulatory proceedings, including lawsuits brought by private litigants, may also follow as a consequence.

Other Applicable Laws

We are subject to a variety of financial disclosure and securities trading regulations, both in the United States and in other jurisdictions in which we operate, as a public company in the U.S., including laws relating to the oversight activities of the SEC and the regulations of the Nasdaq Global Select Market ("Nasdaq"), on which our shares of common stock are traded.

We are also subject to various other federal, state, and local laws and regulations, including those related to safe working conditions, and the storage, transportation, or discharge of items that may be considered hazardous substances, hazardous waste, or environmental contaminants.

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

We are also subject to or affected by federal, state and foreign privacy, security and data protection laws, regulations, standards and regulatory guidance that govern the collection, use, disclosure, retention, security and transfer of personal data. Our operations extend to countries around the world, and many of these jurisdictions have established privacy legal frameworks with which we, our customers or our vendors must comply.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval.

In particular, the Affordable Care Act has had, and is expected to continue to have, a significant impact on the healthcare industry. The Affordable Care Act was enacted to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The law has continued the downward pressure on pharmaceutical pricing, especially under the Medicare program, and increased the industry's regulatory burdens and operating costs. With regard to pharmaceutical products, among other things, the Affordable Care Act revised the definition of "average manufacturer price" ("AMP") for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and imposed a significant annual fee on companies that manufacture or import certain branded prescription drug products.

There remain judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as efforts by the current administration to repeal or replace certain aspects of the Affordable Care Act. Since January 2017, the President of the United States has signed Executive Orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act of 2017, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act's "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax.

Further, the Bipartisan Budget Act of 2018, among other things, amended the Affordable Care Act, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In addition, the federal government eliminated federal cost-sharing reduction ("CSR") payments to insurance companies. The loss of such federal CSR payments has resulted in increased premiums on certain policies issued by qualified health plans under the Affordable Care Act. Moreover, in December 2018, the Centers for Medicare & Medicaid Services ("CMS") published a new final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On April 27, 2020, the United States Supreme Court reversed a Federal Circuit decision that previously upheld Congress' denial of $12 billion in "risk corridor" funding. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act of 2017, the remaining provisions of the Affordable Care Act are invalid as well. In December 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case. It is unclear how such litigation and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act and our business. The Affordable Care Act is likely to continue the downward pressure on pharmaceutical pricing and may also increase our regulatory burdens and operating costs. We continue to evaluate the effect that the Affordable Care Act and its possible repeal and replacement has on our business.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This included further reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2030 unless additional Congressional action is taken. The Coronavirus Aid, Relief and Economic Security Act, or CARES Act, which was signed into law in March 2020 and is designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030. Additionally, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period in which the government may recover overpayments to providers from three to five years.

Further, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the out-of-pocket cost of prescription drugs and reform government program reimbursement methodologies for drugs. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to pharmaceutical product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the current administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the U.S. presidential administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases.

Additionally, on May 11, 2018, the President of the United States previously laid out his administration's "Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs" to reduce the cost of prescription drugs while preserving innovation and cures. The Department of Health and Human Services has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. Congress and the U.S. presidential administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Additionally, on July 24, 2020, President Trump announced four executive orders related to prescription drug pricing that attempt to implement several of the Trump administration proposals, including (i) a policy that would tie certain Medicare Part B drug prices to international drug prices, or the "most favored nation price," the details of which were released on September 13, 2020 and also expanded the policy to cover certain Part D drugs; (ii) an order that directs HHS to finalize the Canadian drug importation proposed rule previously issued by HHS and makes other changes allowing for personal importation of drugs from Canada; (iii) an order that directs HHS to finalize the rulemaking process on modifying the Anti-Kickback Statute safe harbors for discounts for plans, pharmacies, and pharmaceutical benefit managers; (iv) a policy that reduces costs of insulin and epipens to patients of federally qualified health centers. The FDA also recently released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, whether the current regulations, guidance or interpretations will be changed, or what the impact of such changes on our business, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. In addition, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

It is uncertain whether and how future legislation, whether domestic or foreign, could affect prospects for our product candidates or what actions foreign, federal, state, or private payors for health care treatment and services may take in response to any such health care reform proposals or legislation. Adoption of price controls and other cost-containment measures and adoption of more restrictive policies in jurisdictions with existing controls and measures reforms may prevent or limit our ability to generate revenue, attain profitability or commercialize our product candidates.

Moreover, the Drug Supply Chain Security Act imposes obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this legislation, manufacturers are required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, under this legislation, manufacturers have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Coverage and Reimbursement

Sales of our products, if and when approved, will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government healthcare programs, private health insurers and managed care organizations. Third-party payors generally decide which drugs they will cover and establish certain reimbursement levels for such drugs. In particular, in the United States, private health insurers and other third-party payors often provide reimbursement for products and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of our product candidates, and those of any future product candidate, will therefore depend substantially on the extent to which the costs of our product candidates, and those of any future product candidate, will be paid by third-party payors. Additionally, the market for our product candidates, and those of any future product candidate, will depend significantly on access to third-party payors' formularies without prior authorization, step therapy, or other limitations such as approved lists of treatments for which third-party payors provide coverage and reimbursement. Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. As such, coverage and reimbursement for therapeutic products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will likely be a time-consuming process.

Third-party payors are developing increasingly sophisticated methods of controlling healthcare costs and challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs (including drug prices) has become a priority of federal and state governments. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution by generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could limit our net revenue and results. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products once approved as a benefit under their plans or, if they do, the level of reimbursement may not be sufficient to allow us to sell our products on a profitable basis. Decreases in third-party reimbursement for our products once approved or a decision by a third-party payor to not cover our products could reduce or eliminate utilization of our products and have an adverse effect on our sales, results of operations and financial condition. In addition, state and federal healthcare reform measures have been and will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures.

Employees

As of April 30, 2021, we had 42 full-time employees. Our employees are not represented by any collective bargaining unit, and we believe our relations with our employees are good.

Corporate Information

We were originally an exempted limited company incorporated under the laws of Bermuda in October 2014 and were named Axovant Gene Therapies Ltd. from March 2019 until November 2020. In November 2020, we became a Delaware corporation in connection with the Domestication and changed our corporate name to Sio Gene Therapies Inc. Our principal executive office is located at 130 West 42nd Street, 26th Floor, New York, New York 10036, and our telephone number is 1 (877) 746-4891.

Available Information

Our website is www.siogtx.com. The contents of, or information accessible through, our website are not part of this Annual Report on Form 10-K, and our website address is included in this document as an inactive textual reference only. We make our filings with the SEC, including our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports, available free of charge on our website as soon as reasonably practicable after we file such reports with, or furnish such reports to, the SEC. Additionally, the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC's website is www.sec.gov.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products 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, and will continue to rely, upon a combination of patents, trademarks, trade secret protection and confidentiality agreements with employees, consultants, collaborators, advisors and other third parties to protect the intellectual property related to our current and future development programs and product candidates. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries for our current gene therapy product candidates and any future product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our current and future product 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.

The patent applications we have in-licensed or own cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such application(s). Our in-licensed and/or owned patent applications may fail to result in issued patents with claims that cover our current product candidates or other gene therapy product candidates in the United States or in foreign countries. Our in-licensed and owned patent portfolio alone may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our current product candidates or any future product candidates in the United States or in other foreign countries. We may also inadvertently make statements to regulatory agencies during the regulatory approval process that may be inconsistent with positions that have been taken during prosecution of our in-licensed or owned patents which may result in such patents being narrowed, invalidated, or held unenforceable.

The patent rights that we own or have licensed relating to our product candidates may be limited in ways that may affect our ability to exclude third parties from competing against us if we obtain regulatory approval to market these product candidates. For our current product candidates or future product candidates for which we do not hold or do not obtain composition of matter patents, competitors who obtain the requisite regulatory approval can offer products with the same composition as our products so long as the competitors do not infringe any other patents, such as method patents, that we may hold or obtain rights to. Method patents only protect the product when used or sold for the specified method. However, this type of patent protection does not limit a competitor from making and marketing a product that is identical to our product that is labeled for an indication that is outside of the patented method, or for which there is a substantial use in commerce outside the patented method.

There is no assurance that all of the 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 be used to invalidate a patent. The patent examination process may require us to narrow our claims, which may limit the scope of patent protection that we may obtain. Even if patents do successfully issue based on our owned or in-licensed applications and even if such patents cover our current or future product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to us in the future could deprive us of rights necessary for the successful commercialization of any current or future product candidates, if approved. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

Our owned or in-licensed pending applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. If the patent applications we hold or have in-licensed with respect to our development programs and product candidates fail to issue as patents, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our current or future product candidates, it could dissuade companies from collaborating with us to develop product candidates and threaten our ability to commercialize future products. Any such outcome could have an adverse effect on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in 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 owned or licensed patents or pending patent applications, or whether we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. 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.

Patent reform legislation could increase uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents. On September 16, 2011, the Leahy-Smith America Invents Act (the "Leahy-Smith Act") was signed into law. The Leahy-Smith Act made a number of significant changes to United States patent laws. These include provisions that affect the way patent applications are prosecuted and challenged at the U.S. Patent and Trademark Office ("USPTO") and may also affect patent litigation. The USPTO has developed and continues to develop new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act, subsequent rulemaking, and judicial interpretation of the Leahy-Smith Act and regulations will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement and/or defense of our issued patents, all of which could have an adverse effect on our business and financial condition.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our 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.

Even if our patent applications that we own or license issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

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.

The inventorship and/or ownership rights for patents or patent applications we own or in-license may be challenged by third parties. Such challenges could result in loss of exclusive rights to such patents, which could limit our ability to stop others from using or commercializing similar or identical technology and products or require us to obtain a license from such third parties on commercially reasonable terms to secure exclusive rights, or our business could be harmed. If any such challenges to inventorship and/or ownership were asserted, there is no assurance that a court would find in our favor or that, if we choose to seek a license, such license would be available to us on acceptable terms or at all.

Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after the first non-provisional filing date. Certain 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 biosimilar or 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.

If we do not obtain protection under the Hatch-Waxman Amendments by extending the patent term and obtain data exclusivity for our product candidates, our business may be materially harmed.

Our commercial success will largely depend on our ability to obtain and maintain patents and other intellectual property in the United States and other countries with respect to our proprietary technology, product candidates and our target indications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidates might expire before or shortly after such candidates begin to be commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our owned or in-licensed U.S. patents or patent applications, once issued, may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years beyond the normal expiration of the patent as compensation for patent term lost during development and the FDA regulatory review process, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the total patent term including the period of extension cannot exceed 14 years from the product's approval date. Furthermore, this extension is limited to only one patent that covers the approved product, the approved use of the product, or a method of manufacturing the product. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. We may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request.

If we are unable to extend the expiration date of our existing patents or obtain new patents with longer expiry dates, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and nonclinical data to obtain approval of competing products following our patent expiration and launch their product earlier than might otherwise be the case.

The validity, scope and enforceability of any patents that cover our biologic product candidates can be challenged by third parties.

For biologics, such as AXO-AAV-GM1, AXO-AAV-GM2 and AXO-Lenti-PD, the Biologics Price Competition and Innovation Act ("BPCIA") provides a mechanism for one or more third parties to seek FDA approval to manufacture or sell biosimilar or interchangeable versions of brand name biological products. Due to the large size and complexity of biological products, as compared to small molecules, a biosimilar must be "highly similar" to the reference product with "no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product." The BPCIA provides, among other things, for a formal pre-litigation process which includes the exchange of information between a biosimilar applicant and a reference product sponsor that can include the identification of relevant patents and each parties' basis for infringement and invalidity. After the exchange of this information (if the exchange is elected), we must then initiate an infringement lawsuit within 30 days for the patents identified in the exchange. If the biosimilar applicant successfully challenges the asserted patent claims it could result in the invalidation of, or render unenforceable, some or all of the relevant patent claims or result in a finding of non-infringement.

Litigation or other proceedings to enforce or defend intellectual property rights are often complex in nature, may be expensive and time-consuming, may divert our management's attention from our core business, and may result in unfavorable results that could limit our ability to prevent third parties from competing with our product candidates.

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.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and other foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign national or international patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of patent rights include, but are not limited to, failure to timely file national and regional stage patent applications based on our international patent application, failure to respond to office actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our current or future product candidates, our competitors might be able to enter the market sooner, which would have an adverse effect on our business.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third-party may hold intellectual property, including patent rights and trade secrets that are important or necessary to the development of our current or future product candidates. It may be necessary for us to use the patented or proprietary technology of one or more third parties to manufacture or commercialize our product candidates, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially. If any such patents were to be asserted against us, there is no assurance that a court would find in our favor or that, if we choose or are required to seek a license, a license to any of these patents would be available to us on acceptable terms or at all.

It may be necessary to use a patented or proprietary AAV-related technology of one or more third parties to manufacture and commercialize AXO-AAV-GM1 or AXO-AAV-GM2. If we are unable to obtain licenses from such third parties when needed or on commercially reasonable terms, our ability to commercialize AXO-AAV-GM1 (if approved) or AXO-AAV-GM2 (if approved), would likely be delayed or impaired.

Third-party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights may delay or prevent the development and commercialization of our product candidates.

Our commercial success depends in part on our avoiding infringement and other violations of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, derivation and administrative law proceedings, inter partes review, and post-grant review before the USPTO, as well as oppositions and similar proceedings in foreign jurisdictions. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates or other business activities may be subject to claims of infringement of the patent and other proprietary rights of third parties. Third parties may assert that we are infringing their patents or employing their proprietary technology without authorization.

There may be third-party patents or patent applications with claims to compositions, materials, formulations, methods of manufacture or methods for treatment related to our current or future product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our current or future product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates; any molecules, plasmids, vectors, cell lines, etc. formed during the manufacturing process; any final product itself or the intended method of treatment using the product, including combination therapy, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

A license may not be available on commercially reasonable terms or at all. In addition, we may be subject to claims that we are infringing other intellectual property rights, such as trademarks or copyrights, or misappropriating the trade secrets of others, and to the extent that our employees, consultants or contractors use intellectual property or proprietary information owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful infringement or other intellectual property claim against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our affected products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We cannot provide any assurances that third-party patents do not exist which might be enforced against our product candidates, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation to third parties.

Third-party patent applications directed to methods for producing recombinant lentiviral vectors or recombinant AAV vectors could adversely affect the potential commercialization of our current gene therapy product candidates, if patents issue from such applications that include claims that would cover the methods of making our current gene therapy product candidates. While we do not believe that such pending third-party claims that would cover the methods of making our current gene therapy product candidates are likely to be patentable, we may be incorrect in this belief.

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 and market our products.

We cannot guarantee that any of our or our licensors' patent searches or analyses, including the identification of relevant patents, the scope of patent claims or 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 and abroad that is or may be relevant to or necessary for the commercialization of our product candidates in any jurisdiction. Patent applications in the United States and elsewhere are not published until 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. In addition, U.S. patent applications filed before November 29, 2000 and certain U.S. patent applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Therefore, patent applications covering our products could have been filed by others without our knowledge. Additionally, pending patent applications or patents 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 products.

The scope of a patent claim is determined by multiple factors including 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 products. We may incorrectly determine that our products 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 or abroad that we consider relevant may be incorrect, and our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

If we fail to identify and correctly 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 damages, we may be temporarily or permanently prohibited from commercializing any of our products that are held to be infringing. We might, if possible, also be forced to redesign products, processes, or services so that we no longer infringe the 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.

If we breach any of our license or collaboration agreements, it could compromise our development and commercialization efforts for our product candidates.

We have licensed rights to intellectual property from UMMS and Oxford in order to commercialize our product candidates, and we have or intend to enter into one or more commercial supply and manufacturing agreements for our current product candidates.

Disputes may arise between us and any of these counterparties regarding intellectual property rights that are subject to such agreements, including, but not limited to:

- the scope of rights granted under the agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the agreement;
- our right to sublicense patent and other rights to third parties;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners;
- our right to transfer or assign our license; and
- the effects of termination.

These or other disputes over intellectual property that we have licensed (or will license or acquire in the future) may prevent or impair our ability to maintain our current arrangements on acceptable terms or may impair the value of the arrangement to us. Any such dispute could have an adverse effect on our business.

If we materially breach or fail to perform any provision under these license and collaboration agreements, including failure to make payments to a licensor or collaborator when due for royalties and failure to use commercially reasonable efforts to develop and commercialize our product candidates, such licensors and collaborators have the right to terminate our agreement, and upon the effective date of such termination, our right to practice the licensed patent rights and other intellectual property would end. Any uncured, material breach under the agreements could result in our loss of rights to practice the patent rights and other intellectual property licensed to us under the agreements and to liability for potential damages.

Our intellectual property agreements with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology.

Certain provisions in our intellectual property agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could affect the scope of our rights to the relevant intellectual property or technology or affect financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may become involved in lawsuits to protect or enforce our patents, the patents of our licensors or our other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. The initiation of a claim against a third-party may also cause the third-party to bring counter claims against us such as claims asserting that our patents are invalid or unenforceable.

In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement, or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post-grant proceedings such as ex parte reexaminations, inter partes review, or post-grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third-party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could harm our business.

We may not be able to detect or prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common stock.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third-party is infringing our issued patent, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

The United States has recently enacted and implemented wide-ranging patent reform legislation. 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. 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 actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future.

The United States government may have certain rights in patent applications and patents issuing therefrom that we in-license or own. The United States federal government retains certain rights in inventions produced with its financial assistance under the Bayh-Dole Act. The federal government retains a “nonexclusive, nontransferable, irrevocable, paid-up license” for its own benefit. The Bayh-Dole Act also provides federal agencies with “march-in rights.” March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.” If the patent owner refuses to do so, the government may grant the license itself. Furthermore, if the U.S. Government has rights related to a product candidate under the Bayh-Dole Act, we may be obligated to substantially manufacture in the U.S. such product if it was invented using government funding. Under certain circumstances, we may be able to obtain a waiver to manufacture outside the U.S., however, such waivers are not guaranteed.

We may not be able to protect our intellectual property rights throughout the world, which could impair our business.

Filing, prosecuting and defending patents covering our current and future product candidates throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents and any future patent claims, or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of some countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

Many countries, including EU countries, India, Japan and China, have compulsory licensing laws under which a patent owner may be compelled under specified circumstances to grant licenses to third parties. In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third-party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we expect to rely on third parties to manufacture our product candidates, and we expect to continue to collaborate with third parties on the development of our current and future product candidates, we must, 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 collaboration or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants 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. Despite the contractual provisions employed when working with 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. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Further, adequate remedies may not exist in the event of unauthorized use or disclosure. Given that our proprietary 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.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Policing unauthorized use of our or our licensors' intellectual property is difficult, expensive and time-consuming, and we may be unable to determine the extent of any unauthorized use. Moreover, enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. Although we seek to protect our ownership of intellectual property rights by ensuring that our agreements with our employees, collaborators, and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we or our licensors fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we and our licensors are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

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, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to initiate or continue our clinical trials and internal research programs, or in-license needed technology or other product candidates. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace, including compromising our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development collaborations that would help us commercialize our product candidates, if approved.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our current and future product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Any trademarks we have obtained or may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. Once we select new trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks and we may not have adequate resources to enforce our trademarks.

If we attempt to enforce our trademarks and assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Intellectual property rights 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 or other intellectual property rights that we own or that we have exclusively licensed and have the right to enforce;
- we, our licensor or any collaborators might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or license;
- we or our licensor might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; and
- we may not develop additional proprietary technologies that are patentable.

Item 1A. Risk Factors

You should carefully consider the following risk factors, in addition to the other information contained in this Annual Report on Form 10-K, including the section of this report titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties of which we are unaware, or that we currently believe are not material, may also become important factors that adversely affect our business. If any of the events described in the following risk factors and the risks described elsewhere in this report occurs, our business, operating results and financial condition could be seriously harmed and the trading price of our shares of common stock could decline. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this report. See the section under Part I of this report titled "Cautionary Note Regarding Forward-Looking Statements".

Risks Related to Our Business, Financial Position and Capital Requirements

We have a limited operating history and have never generated any product revenues.

We are a clinical-stage gene-therapy company with a limited operating history. Our operations to date have been limited to organizing and staffing our company, raising capital, acquiring product candidates and advancing our product candidates into clinical development. We have not yet demonstrated an ability to successfully complete a registration-enabling pivotal clinical trial, obtain marketing approval, manufacture a clinical-stage or commercial-scale product, or arrange for a third-party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, we have no meaningful operations upon which to evaluate our business and 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 pharmaceutical products.

In addition, the failure of our clinical trials for and the discontinuation of development of intepirdine and nelotanserin has required us to reevaluate our business and led to dramatic shifts in our strategy and business plan. Our new strategy and business plan have not yet been proven and we may never be successful in developing or commercializing any of our gene therapy product candidates, including our gene therapy product candidates, which remain in early stages of clinical development.

Our ability to generate revenue and become profitable depends upon our ability to successfully complete the development of our product candidates and to obtain the necessary regulatory approvals for their commercialization. We have never been profitable, have not generated any revenue from product sales, and have no products approved for commercial sale.

Even if we receive regulatory approval for our product candidates, we do not know when those candidates will generate revenue, if at all. Our ability to generate product revenue depends on a number of factors, including our ability to:

- successfully commence and complete clinical trials and obtain regulatory approval for the marketing of our gene therapy product candidates;
- establish effective sales, marketing and distribution systems for our gene therapy product candidates;
- add operational, financial and management information systems and personnel, including personnel to support our clinical, manufacturing and planned future commercialization efforts and operations as a public company;
- initiate and continue relationships with third-party suppliers and manufacturers, including Oxford Biomedica (UK) Ltd. ("Oxford"), Viralgen Vector Core, S.L. and other third-party cGMP manufacturers, and have clinical and commercial quantities of our gene therapy product candidates manufactured at acceptable cost and quality levels;
- attract and retain an experienced management and advisory team;
- raise additional funds when needed and on terms acceptable to us;
- achieve broad market acceptance of our products in the medical community and with third-party payors and consumers;
- launch commercial sales of our products, whether alone or in collaboration with others;
- compete effectively with other biotechnology and gene therapy companies targeting neurological diseases; and
- obtain, maintain, expand and protect necessary intellectual property rights.

Because of the numerous risks and uncertainties associated with product 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. Our expenses could increase beyond expectations if we are required by the United States Food and Drug Administration ("FDA"), European Medicines Agency ("EMA"), Japan's Pharmaceutical and Medical Devices Agency ("PMDA") or comparable regulatory authorities in other countries, to perform studies or clinical trials in addition to those that we currently anticipate. Even if our product candidates are approved for commercial sale, we anticipate incurring significant costs associated with their commercial launch. If we cannot successfully execute any one of the foregoing, our business may not succeed, and your investment will be adversely affected.

Our business, operations and clinical development plans and timelines could continue to be adversely impacted by the effects of health epidemics, including the recent COVID-19 pandemic, on the manufacturing, clinical trial and other business activities performed by us or by third parties with whom we conduct business, including our contract manufacturers, contract research organizations, or CROs, shippers and others.

Our business, including patient enrollment and Chemistry, Manufacturing and Controls ("CMC") manufacturing efforts for our clinical trials, could continue to be adversely impacted by health epidemics wherever we have clinical trial sites or other business operations. In addition, health epidemics could cause significant disruption in the operations of third-party manufacturers, CROs and other third parties upon whom we rely. For example, the global COVID-19 pandemic and measures introduced by local, state and federal governments to contain the virus and mitigate its public health effects have significantly impacted and may continue to significantly impact our industry and the global economy. These and similar, and perhaps more severe, disruptions in our operations, our industry and the global economy could negatively impact our business, operating results and financial condition.

We are dependent on an international supply chain for products to be used in our clinical trials and, if approved by the regulatory authorities, for commercialization. Continued quarantines, shelter-in-place and similar government orders, whether related to COVID-19 or other infectious diseases, could impact personnel at third-party manufacturing facilities or the availability or cost of materials, which could disrupt our supply chain. Any manufacturing supply interruption of our product candidates could harm our ability to conduct ongoing and future clinical trials of our product candidates. In addition, closures of transportation carriers and modal hubs could materially impact our clinical development and any future commercialization timelines.

If our relationships with our suppliers or other vendors are terminated or scaled back as a result of the COVID-19 pandemic or other health epidemics, we may not be able to enter into arrangements with alternative suppliers or vendors or do so on commercially reasonable terms or in a timely manner. Switching or adding additional suppliers or vendors involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new supplier or vendor commences work. As a result, delays occur, which could adversely impact our ability to meet our desired clinical development and any future commercialization timelines. Although we carefully manage our relationships with our suppliers and vendors, 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.

In addition, our clinical trials have been affected by the COVID-19 pandemic. Clinical trial progression, dosing, patient enrollment and related activities have been delayed due to concerns among patients about participating in clinical trials during a pandemic, and reporting of some clinical data may be incomplete or delayed if patients enrolled in our clinical trials are unable to fully participate in all necessary measurement protocols as a result of any such hospital resource prioritization, patient participation concerns or other factors associated with the COVID-19 pandemic. Federal, state, and local guidelines for reopening in the United States and United Kingdom, where our clinical trials are being run, may negatively impact our ability to enroll additional patients in any of our clinical programs. Some patients may have difficulty following certain aspects of clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. For example, patients in our clinical trials for AXO-AAV-GM1 and AXO-AAV-GM2 are infants, often with advanced disease, who may not be able to safely participate in clinical trials for these product candidates during the COVID-19 pandemic or if they have not or are not eligible to receive COVID-19 vaccinations. Additionally, our clinical trial for AXO-Lenti-PD can involve elderly patients with advanced disease who may be unable to participate in clinical assessments at our research sites in the United Kingdom. For example, because of the COVID-19 pandemic and a patient refusal, two out of four patients in the second cohort of our Phase 2 clinical trial of AXO-Lenti-PD at our United Kingdom clinical trial sites were unable to participate in Unified Parkinson's Disease Rating Scale assessments and the mandatory washout of background levodopa therapy at the six-month time point. However, all four of these subjects were able to complete all other efficacy assessments at the six-month timepoint, including the patient-recorded Hauser diaries. We are working with sites and investigators to ensure safe and ethical data collection at future time points through the pandemic in accordance with regulatory guidance. Similarly, our inability to successfully recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 or experience additional restrictions by their institutions or local, state or national governments, could adversely impact our clinical trial operations.

The ultimate impact and evolving effects of the COVID-19 pandemic or a similar health epidemic are highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could harm our operations, and we will continue to monitor the COVID-19 situation closely.

We expect to incur significant losses for the foreseeable future and may never achieve or maintain profitability.

Investment in pharmaceutical and biological product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to gain regulatory approval or become commercially viable. We have never generated any revenues, and we cannot estimate with precision the extent of our future losses. We do not currently have any products that are available for commercial sale and we may never generate revenue from selling products or achieve profitability. We expect to continue to incur substantial and increasing losses through the projected commercialization of our product candidates. Our product candidates have not been approved for marketing in the United States or any other jurisdiction, and we may never receive any such approvals. We are uncertain when or if we will achieve profitability and, if so, whether we will be able to sustain it. Our ability to produce revenue and achieve profitability is dependent on our ability to complete the development of our product candidates, obtain necessary regulatory approvals, and have our product candidates manufactured and successfully marketed and commercialized. We cannot assure you that we will be profitable even if we successfully commercialize our product candidates. If we do successfully obtain regulatory approval to market our product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the number of competitors in such markets, the accepted price for our product candidates and whether we own the commercial rights for that territory. If the indication approved by regulatory authorities is narrower than we expect, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of our product candidates, even if approved. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Failure to become and remain profitable may adversely affect the market price of our common stock and our ability to raise capital and continue operations.

We expect our research and development expenses to be significant as we develop our gene therapy product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur increased sales and marketing expenses. As a result, we expect to continue to incur significant operating losses and negative cash flows from operations for the foreseeable future. These losses have had and will continue to have an adverse effect on our financial position and working capital.

We estimate that our current cash and cash equivalents balance is sufficient to support operations beyond the twelve-month period following the date that the accompanying consolidated financial statements were issued, including beyond the expected dates of major upcoming milestones for our AXO-AAV-GM1 gene therapy program for the treatment of GM1 gangliosidosis. As such, we have determined that there is no longer substantial doubt about our ability to continue as a going concern for the one-year period following the date that the accompanying consolidated financial statements were issued. These estimates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

In order to meet our long-term operating requirements, we will need, among other things, additional capital resources. We continually assess multiple options to obtain additional funding to support our operations, including proceeds from offerings of our equity securities or debt, or transactions involving product development, technology licensing or collaboration arrangements, or other sources of capital to complete our currently planned development programs. Sources of a sufficient amount of financing may not be available to us on favorable terms, if at all, and our ability to raise additional capital may be adversely impacted by potentially worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates. Any significant delays in our programs may also require us to reevaluate our corporate strategy, resulting in the expenditure of significant resources and time, or potentially resulting in us discontinuing our operations.

We are heavily dependent on the success of our gene therapy product candidates, which are still in early stages of clinical or preclinical development. If we are unable to successfully develop and commercialize any of our product candidates, our business will be harmed.

We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to the development of our gene therapy product candidates, all of which are in the early stages of clinical development. Accordingly, our business currently depends heavily on the successful development, regulatory approval and commercialization of these product candidates. We cannot be certain that any of our product candidates will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of our product candidates are and will remain subject to extensive regulation by the FDA, the EMA, the PMDA and other comparable regulatory authorities that each have differing regulations. We are not permitted to market our product candidates in the United States or in any foreign countries until they receive the requisite approvals from the FDA or comparable regulatory authorities in other countries. We have not submitted marketing applications to the FDA or foreign regulatory authorities and do not expect to be in a position to do so for the foreseeable future. Obtaining marketing approval is a lengthy, expensive and inherently uncertain process, and regulatory authorities may delay, limit or deny approval of our product candidates for many reasons, including:

- we may not be able to demonstrate that a product candidate is safe and effective as a treatment for our targeted indications to the satisfaction of the applicable regulatory authorities;
- our BLA or other key regulatory filings may be delayed or rejected due to issues, including those related to product quality and manufacturing, timing of results from supporting studies, database lock and data transfer;
- the regulatory authorities may require additional nonclinical studies or clinical studies of the product candidate in Parkinson’s disease or other indications, which would increase our costs and prolong our development;
- the results of our clinical trials may not meet the level of statistical or clinical significance required for marketing approval;
- the regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the contract research organizations ("CROs") that we retain to conduct clinical trials may take actions outside of our control, or otherwise commit errors or breaches of protocols, that adversely impact our clinical trials;
- the regulatory authorities may not find the data from nonclinical studies and clinical trials sufficient to demonstrate that the clinical and other benefits of the product candidate outweigh its safety risks;
- the regulatory authorities may disagree with our interpretation of data from our nonclinical studies and clinical trials or may require that we conduct additional studies;
- the regulatory authorities may not accept data generated at our clinical trial sites;

- the regulatory authorities may require, as a condition of approval, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a risk evaluation and mitigation strategy ("REMS") as a condition of approval;
- the regulatory authorities may identify deficiencies in the manufacturing processes or facilities of our third-party manufacturers; or
- the regulatory authorities may change their approval policies or adopt new regulations.

In addition, in October 2020, our manufacturing partner for AXO-Lenti-PD, Oxford, informed us of delays in CMC data and third-party fill/finish issues. As a result, the development of a suspension-based manufacturing process for AXO-Lenti-PD has taken longer than expected, which will likely result in delays in starting our planned randomized, sham-controlled trial of AXO-Lenti-PD. There can be no assurance as to the timeline for our planned trial or that we will not experience future delays, which would adversely affect our business, financial condition and results of operations.

We will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of our product candidates.

We are currently in the clinical stage of operations and have not yet achieved profitability. We expect to continue to incur significant operating and net losses, as well as negative cash flows from operations, for the foreseeable future as we continue to develop our gene therapy product candidates and prepare for potential future regulatory approvals and commercialization of our products. We have not generated any revenue to date and do not expect to generate product revenue unless and until we successfully complete development and obtain regulatory approval for at least one of our gene therapy product candidates. Our current cash and cash equivalents balance will also not be sufficient to complete all necessary development activities and commercially launch our products.

We expect to spend substantial amounts to complete the development of, seek regulatory approvals for and commercialize our product candidates. Because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. However, we anticipate that our current cash and cash equivalents balance is sufficient to fund our clinical milestones beyond the expected dates of major upcoming milestones for our AXO-AAV-GM1 gene therapy program for the treatment of GM1 gangliosidosis. 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 trials of our product candidates;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, the EMA, or the PMDA, and other comparable foreign regulatory authorities;
- the achievement of certain development, regulatory and commercialization milestones that give rise to milestone and royalty payments to licensors;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of obtaining necessary intellectual property and defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates or any future product candidates;
- the effect of competing technological and market developments;
- the cost and timing of completion of clinical-stage and commercial-scale manufacturing activities, including costs that may result from delays in the development of a suspension-based manufacturing process by our partner, Oxford;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates in regions where we choose to commercialize our products on our own; and
- the initiation, progress, timing and results of our commercialization of our product candidates, if approved for commercial sale.

For the years ended March 31, 2021 and March 31, 2020, we incurred net losses of $32.4 million and $72.6 million, respectively. As of March 31, 2021, our cash and cash equivalents totaled $119.0 million and our accumulated deficit was $791.1 million. We estimate that our current cash and cash equivalents balance is sufficient to support operations beyond the twelve-month period following the date that the accompanying consolidated financial statements were issued, including beyond the expected dates of major upcoming milestones for our AXO-AAV-GM1 gene therapy program for the treatment of GM1 gangliosidosis. As such, we have determined that there is no longer substantial doubt about our ability to continue as a going concern for the one-year period following the date that the accompanying consolidated financial statements were issued. These estimates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

In order to meet our long-term operating requirements, we will need, among other things, additional capital resources. We continually assess multiple options to obtain additional funding to support our operations, including proceeds from offerings of our equity securities or debt, or transactions involving product development, technology licensing or collaboration arrangements, or other sources of capital to complete our currently planned development programs. Sources of a sufficient amount of financing may not be available to us on favorable terms, if at all, and our ability to raise additional capital may be adversely impacted by potentially worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates. Any significant delays in our programs may also require us to reevaluate our corporate strategy, resulting in the expenditure of significant resources and time, or potentially resulting in us discontinuing our operations.

Raising additional funds by issuing securities may cause dilution to existing stockholders, raising additional funds through debt financings may involve restrictive covenants, and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

We expect that significant additional capital will be needed in the future to continue our planned operations. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, strategic alliances and license and development agreements in connection with any collaborations. We do not have any committed external source of funds. To the extent that we raise additional capital by issuing equity securities, including pursuant to our "shelf" registration statement filed with the U.S. Securities and Exchange Commission (the "SEC") and our "at-the-market" offering of common stock, our existing stockholders' ownership may experience substantial dilution, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing or preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise develop and market ourselves.

We may be required to make significant payments to third parties under the agreements pursuant to which we acquired our gene therapy product candidates.

Under our agreements with UMMS and Oxford, we are subject to significant obligations, including payment obligations upon achievement of specified milestones and payments based on product sales, as well as other material obligations. Some of these milestones require us to make payments prior to generating any product sales. We may not have sufficient funds available to meet our obligations at such time as any of these payments become due, in which case our development efforts would be harmed. Further, failure to make these payments or to meet our other material obligations may result in our counterparties pursuing various remedies under those agreements that could harm our operations.

Our business plan may lead to the initiation of one or more gene therapy development programs, the discontinuation of one or more development programs, or the execution of one or more transactions that you do not agree with or that you do not perceive as favorable to your investment.

In June 2018, we announced that we received from Oxford a worldwide exclusive license to develop and commercialize AXO-Lenti-PD and its predecessor product candidate ProSavin and related gene therapy products (the "Oxford Agreement"). In July 2018, we announced that we received from Benitec Biopharma Limited ("Benitec") a worldwide exclusive license to develop and commercialize investigational gene therapy AXO-AAV-OPMD and related gene therapy products (the "Benitec Agreement"). In December 2018, we announced that we had received from the University of Massachusetts Medical School ("UMMS") a worldwide exclusive license to develop and commercialize gene therapy product candidates AXO-AAV-GM1 and AXO-AAV-GM2 (the "UMMS Agreement"). We are pursuing a strategy to leverage our clinical experience and expertise for the clinical development and regulatory approval of our gene therapy product candidates. As part of our ongoing business strategy, we continue to explore potential opportunities to acquire or license new product candidates and to collaborate on our existing products in development.

We cannot be certain that our product candidates will be successfully developed, or that the early clinical trial results of these product candidates will be predictive of future clinical trial results. We may determine at any time that one or more of our in-licensed product candidates is not suitable for continued development due to cost, feasibility of obtaining regulatory approvals or any other reason, and may terminate the related license. For example, in June 2019, we decided to terminate the Benitec Agreement following our decision to no longer pursue development of AXO-AAV-OPMD and related gene therapy product candidates. In addition, we have limited data from small, uncontrolled clinical trials, performed by or on behalf of Oxford, regarding the safety and tolerability of ProSavin, as the predecessor product candidate to AXO-Lenti-PD, in patients with advanced Parkinson’s disease, as well as nonclinical in vitro experiments with AXO-Lenti-PD. Prior ProSavin trials were not powered to demonstrate the efficacy of the therapy with statistical significance. Given the information above, these trials could be underpowered to demonstrate a potential clinical benefit for AXO-Lenti-PD in these indications.

This business plan requires us to be successful in a number of challenging, uncertain and risky activities, including pursuing development of our gene therapy product candidates in indications for which we have limited or no human clinical data, designing and executing a nonclinical and/or clinical development program for our product candidates, building internal or outsourced gene therapy capabilities, converting early stage gene therapy research efforts into clinical development opportunities, identifying additional promising new assets for development that are available for acquisition or in-license and that fit our strategic focus and identifying potential partners to collaborate on our products. We may not be successful at one or more of the activities required for us to execute this business plan. In addition, we are also continuing to consider other strategic alternatives, such as mergers, acquisitions, divestitures, joint ventures, partnerships and collaborations. We cannot be sure when or if any type of transaction will result. Even if we pursue a transaction, such transaction may not be consistent with our stockholders’ expectations or may not ultimately be favorable for our stockholders, either in the shorter or longer term.

Our growth prospects and the future value of our company are primarily dependent on the progress of our ongoing and planned clinical development programs for our product candidates as well as the outcome of our ongoing business development efforts and pipeline expansion activities, together with the amount of our remaining available cash. The development of our product candidates and the outcome of our ongoing business development efforts and pipeline expansion activities are highly uncertain.

We expect to continue to reassess and make changes to our existing development programs and pipeline expansion strategy. Our plans for our development programs may be affected by the results of competitors’ clinical trials of product candidates addressing our current target indications, and our business development efforts and pipeline expansion activities may also be affected by the results of competitors' ongoing research and development efforts. We may modify, expand or terminate some or all of our development programs, clinical trials or collaborative research programs at any time as a result of new competitive information or as the result of changes to our product pipeline or business development strategy.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel. In addition, if we are unable to effectively transition and integrate our new executive officers, our business and financial performance could be adversely affected.

We may not be able to attract or retain qualified management and commercial, scientific and clinical personnel due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our financial performance will depend in significant part on our senior management team and key employees with expertise in the gene therapy development field. We are highly dependent on the skills and leadership of our management team. Our senior management and key employees may terminate their position with us at any time. If we lose one or more members of our senior management team or key employees, our ability to successfully implement our business strategy could be seriously harmed. Replacing these individuals may be difficult, cause disruption, 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 products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate additional key personnel. We do not maintain "key person" insurance for any of our executives or other employees.

Many of the other biopharmaceutical 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. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates and consultants than what we have to offer. 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, our ability to effectively manage any future growth and our business will be limited.

Our employees, independent contractors, principal investigators, consultants, commercial collaborators, manufacturers, service providers and other vendors, or those of our affiliates, may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.

Our employees and contractors, including principal investigators, consultants, commercial collaborators, manufacturers, service providers and other vendors, or those of our affiliates, may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or other unauthorized activities that violate the laws and regulations, including those of the FDA and other similar regulatory bodies that require the reporting of true, complete and accurate information; manufacturing standards; federal, state and foreign healthcare fraud and abuse laws and data privacy; or laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing, bribery, corruption, antitrust violations, and other abusive practices. These laws may restrict or prohibit a wide range of business activities, including research, manufacturing, distribution, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in nonclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee or third-party misconduct, 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 be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government agency could allege such fraud or other misconduct, even if none occurred. If our employees, independent contractors, principal investigators, consultants, commercial collaborators, manufacturers, service providers or other vendors, or those of our affiliates, are alleged or found to be in violation of any such regulatory standards or requirements, or become subject to a corporate integrity agreement or similar agreement and curtailment of our operations, it could have a significant impact on our business and financial results, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, suspension or delay in clinical trials, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, FDA debarment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight, any of which could adversely affect our ability to operate our business and our results of operations.

Operation of our business internationally exposes us to business, regulatory, political, operational, financial and economic risks associated with doing business in various jurisdictions globally.

Our business strategy includes establishing and maintaining operations and certain key third party arrangements in various jurisdictions around the world. Doing business internationally involves a number of risks, including:

- multiple, conflicting and changing laws and regulations such as tax laws, export and import restrictions, employment laws, anti-bribery and anti-corruption laws, regulatory requirements and other governmental approvals, permits and licenses;

- failure by us or our distributors to obtain appropriate licenses or regulatory approvals for the sale or use of our product candidates, if approved, in various countries;

- difficulties in managing foreign operations;
- unexpected changes in tariffs or trade barriers;
- complexities associated with managing multiple payor-reimbursement regimes or self-pay systems;
- financial risks, such as longer payment cycles, difficulty enforcing contracts and collecting accounts receivable and exposure to foreign currency exchange rate fluctuations;
- reduced protection for intellectual property rights;
- reduced protection of contractual rights in the event of bankruptcy or insolvency of the other contracting party;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, including the recent COVID-19 pandemic and related shelter-in-place orders, travel, social distancing and quarantine policies, boycotts, curtailment of trade and other business restrictions;
- failure to comply with foreign laws, regulations, standards and regulatory guidance governing the collection, use, disclosure, retention, security and transfer of personal data, including the European Union General Data Privacy Regulation ("GDPR"); and
- failure to comply with the United Kingdom Bribery Act 2010 ("U.K. Bribery Act") and similar anti-bribery and anti-corruption laws in other jurisdictions, and the Foreign Corrupt Practices Act, including its books and records provisions and its anti-bribery provisions, including by failing to maintain accurate information and control over sales and distributors' activities.

Any of these risks, if encountered, could significantly harm our current or future international operations and, consequently, negatively impact our financial condition, results of operations and cash flows.

The withdrawal of the United Kingdom, or the U.K., from the European Union, or the E.U., commonly referred to as "Brexit", may adversely impact our ability to obtain regulatory approvals of our product candidates in the U.K. or the EU and may require us to incur additional expenses to develop and commercialize our product candidates in the U.K. or the EU or receive clinical supply of our product candidates from manufacturing partners in the U.K.

Following the result of a referendum in 2016, the U.K. left the E.U. on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the U.K. and the E.U., the U.K. was subject to a transition period until December 31, 2020 (the "Transition Period"), during which E.U. rules continued to apply. A trade and cooperation agreement (the "Trade and Cooperation Agreement") that outlines the future trading relationship between the United Kingdom and the European Union was agreed in December 2020.

Since a significant proportion of the regulatory framework in the U.K. applicable to our business and our product candidates is derived from EU directives and regulations, Brexit has had, and may continue to have, a material impact upon the regulatory regime with respect to the development, approval and commercialization of our product candidates in the U.K. or the EU. For example, Great Britain is no longer be covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA, and a separate marketing authorization will be required to market our product candidates in Great Britain. It is currently unclear whether the Medicines & Healthcare products Regulatory Agency in the U.K. is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals, would delay or prevent us from commercializing our product candidates in the U.K. or the E.U. and restrict our ability to generate revenue and achieve and sustain profitability. We anticipate that Oxford, which is based in the U.K., will continue to provide clinical and commercial supply for our AXO-Lenti-PD program. Brexit could affect the clearance or timing of the release of our clinical trial materials out of the U.K. Any such delays could result in our clinical study sites outside of the U.K. not having sufficient clinical trial materials and could adversely affect the timing and completion of our clinical trials.

While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the U.K. and the E.U. there may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Further, should the U.K. diverge from the E.U. from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. We could therefore, both now and in the future, face significant additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the U.K. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the E.U.

Use of social media platforms presents new risks.

We believe that our potential patient population is active on social media. Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the effectiveness of, or adverse experiences with, a product candidate, which could result in reporting obligations. In addition, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us or our product candidates on any social networking website. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business.

The failure to maintain our current enterprise resource planning system ("ERP") could adversely impact our business and results of operations.

If our ERP system does not continue to operate as intended, the effectiveness of our internal controls over financial reporting could be adversely affected or our ability to assess those controls adequately could be delayed. Significant delays in documenting, reviewing and testing our internal control could cause us to fail to comply with our SEC reporting obligations related to our management's assessment of our internal control over financial reporting.

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

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

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

The product liability insurance we currently carry, and any additional product liability insurance coverage we acquire in the future, may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could cause our stock 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.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

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

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would harm our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could harm our business.

The COVID-19 pandemic has also resulted in the FDA imposing preventive measures, including postponements of non-U.S. manufacturing and product inspections. If global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

If we fail to comply with applicable U.S. and foreign privacy and data protection laws and regulations, we may be subject to liabilities that adversely affect our business, operations and financial performance.

We are subject to laws and regulations requiring that we take measures to protect the privacy and security of certain information we gather and use in our business. For example, the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and its implementing regulations impose, among other requirements, certain regulatory and contractual requirements regarding the privacy and security of personal health information. In addition to HIPAA, numerous other federal and state laws, including, without limitation, state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, and storage of personal information. In addition, in June 2018, California enacted the California Consumer Privacy Act ("CCPA") which took effect on January 1, 2020. The CCPA gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that may increase data breach litigation. Although the CCPA includes exemptions for certain clinical trials data, and HIPAA protected health information, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. The CCPA has prompted a number of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business.

We may also be subject to or affected by laws and regulations globally, including regulatory guidance, governing the collection, use, disclosure, security, transfer and storage of personal data, such as information that we collect about patients and healthcare providers in connection with clinical trials and our other operations in the U.S. and abroad. The global legislative and regulatory landscape for privacy and data protection continues to evolve, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. For example, the EU has adopted the GDPR, which introduces strict requirements for processing personal data. The GDPR is likely to increase the compliance burden on us, including by mandating potentially burdensome documentation requirements and granting certain rights to individuals to control how we collect, use, disclose, retain and leverage information about them. The processing of sensitive personal data, such as physical health conditions, may impose heightened compliance burdens under the GDPR and is a topic of active interest among foreign regulators. In addition, the GDPR provides for breach reporting requirements, more robust regulatory enforcement and fines of up to 20 million euros or up to 4% of annual global revenue. While the GDPR affords some flexibility in determining how to comply with the various requirements, significant effort and expense has been, and will continue to be, invested to ensure continuing compliance. Moreover, the requirements under the GDPR may change periodically or may be modified by EU national law and could have an effect on our business operations if compliance becomes more costly than under current requirements.

It is possible that each of these privacy laws may be interpreted and applied in a manner that is inconsistent with our practices. Further, Brexit has created uncertainty with regard to data protection regulation in the U.K. In particular, it is unclear whether, post Brexit, the U.K. will enact data protection legislation equivalent to the GDPR and how data transfers to and from the U.K. will be regulated. Any failure or perceived failure by us to comply with federal, state, or foreign laws or self-regulatory standards could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions and consequences for noncompliance are rising. 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.

We may not be successful in our efforts to identify and acquire additional gene therapy product candidates, or to enter into collaborations or strategic alliances for the development and commercialization of any such future product candidates.

Part of our strategy involves the business development activities of identifying and acquiring 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:

- pre-clinical and early clinical results of any product candidates we acquire may not be predictive of future clinical results;
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance; or
- potential product candidates may not be effective in treating their targeted diseases.

In addition, the process of identifying and acquiring product candidates is highly competitive, and our ability to compete successfully is impacted by the fact that many of the companies with which we compete for these candidates have significantly greater experience, development and commercialization capabilities, name recognition and financial and human resources than we do. Further, our business development efforts are led by our senior executive officers and other management team members and would be significantly impaired if we were to lose the services of any of these executives. The time and resources spent on business development activities may also distract management's attention from our other development and business activities. Even if we are successful in identifying and acquiring additional product candidates, we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. If we are unable to identify and acquire suitable product candidates for clinical development, this could adversely impact our business strategy, our financial position and stock price.

We may also decide to collaborate with other pharmaceutical companies for the development and potential commercialization of our product candidates in the United States or other countries or territories of the world. We will face significant competition in seeking appropriate collaborators. We may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. If and when we collaborate with a third party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate to the third party. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of a number of factors.

Risks Related to Clinical Development, Regulatory Approval and Commercialization

Clinical trials are expensive, time-consuming, difficult to design and implement and involve an uncertain outcome.

Our gene therapy product candidates are still in development and will require extensive clinical testing before we are prepared to submit an application for marketing approval to regulatory authorities. We cannot predict with any certainty if or when we might submit any such application for regulatory approval for our product candidates or whether any such application will be approved by the applicable regulatory authority in our target markets. Human clinical trials are expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. For instance, regulatory authorities may not agree with our proposed endpoints for any clinical trials of our gene therapy product candidates, which may delay the commencement of our clinical trials. The clinical trial process is also time-consuming. We estimate that clinical trials of our product candidates will take at least several years to complete.

Failure can occur at any stage of our clinical trials, and we could encounter problems that cause us to abandon or repeat clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through nonclinical studies and initial clinical trials, and the results of smaller nonclinical or early clinical trials therefore may not be predictive of the results of large scale or later-stage clinical programs. For example, we have discontinued further clinical development of product candidates that did not meet their primary efficacy endpoints in Phase 2, Phase 2b and Phase 3 clinical studies. Likewise, there can be no assurance that the results of studies conducted by collaborators or other third parties will be viewed favorably or are indicative of our own future study results. A number of companies in the biopharmaceutical industry, and especially in the neurology field, have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials, and in the regulatory approval process.

Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development. Any such failures or delays could negatively impact our business, financial condition, results of operations and prospects.

All of our gene therapy product candidates are in early stages of development. The outcome of nonclinical testing and early clinical trials may not be predictive of the success of later stage clinical trials, interim results of a clinical trial do not necessarily predict final results and results from one completed clinical trial may not be replicated in a subsequent clinical trial with a similar study design. The clinical trials conducted to date for our gene therapy product candidates have involved a small number of patients, making it difficult to predict whether the favorable results that we observed in such trials will be repeated in larger and more advanced clinical trials. In addition, the design of a clinical trial, such as endpoints, inclusion and exclusion criteria, statistical analysis plans, data access protocols and trial sizing, 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. Furthermore, as we are exploring new disease areas without any approved treatments, we may need to qualify new and unproven endpoints as we are continuing the development of our product candidates, which may increase uncertainty.

The commencement and completion of clinical trials may be delayed by several factors, including:

- failure to obtain regulatory approval to commence a trial;
- unforeseen safety issues;
- determination of dosing issues;
- lack of effectiveness during clinical trials;
- inability to reach agreement on acceptable terms with prospective CROs and clinical trial sites;
- slower than expected rates of patient recruitment or failure to recruit suitable patients to participate in a trial;
- changes in or modifications to clinical trial design;
- failure to manufacture or obtain supply of sufficient quantities of a gene therapy product candidate or placebo or failure to obtain sufficient quantities of concomitant medication for use in clinical trials;
- inability to monitor patients adequately during or after treatment;
- inability or unwillingness of medical investigators to follow our clinical and other applicable protocols;
- failure to establish sufficient number of clinical trial sites; or
- clinical sites or others deviating from trial protocol, inappropriately unblinding results, or dropping out of a trial.

Further, by way of example, we, a regulatory agency or an institutional review board ("IRB") at a clinical trial site may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA's current Good Clinical Practice ("cGCP") regulations, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our IND submissions or the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of clinical trials. 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 gene therapy product candidates could be harmed, and our ability to generate revenues may be delayed. In addition, any delays in our clinical trials could increase our costs, cause a drop in our stock price, slow down the approval process and jeopardize our ability to commence product sales and generate revenues. In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in commencing or completing clinical trials. Any of these occurrences may harm our business, financial condition and results of operations.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the applicable regulatory agency, which may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The applicable regulatory agency may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the applicable regulatory agency and may ultimately lead to the denial of marketing approval of one or more of our gene therapy product candidates.

In addition, we acquired worldwide rights to our gene therapy product candidates and were not involved in their development prior to such acquisitions. More particularly, we have had no involvement with or control over the nonclinical and clinical development of our gene therapy product candidates prior to acquiring the rights to them. We are dependent on our predecessors, including UMMS and Oxford, having conducted such research and development in accordance with the applicable protocols, legal, regulatory and scientific standards, having accurately reported the results of all clinical trials and other research conducted prior to our acquisition of the gene therapy product candidates, having correctly collected and interpreted the data from these trials and other research and having supplied us with complete information, data sets and reports required to adequately demonstrate the results reported through the date of our acquisition of these assets. In addition, we have limited data regarding the safety, tolerability and efficacy of our gene therapy product candidates and their potential indications, and we have not previously conducted development activities for a biological product candidate. Problems related to our predecessors, including UMMS and Oxford, and our limited available data for our gene therapy product candidates could result in increased costs and delays in the development of our gene therapy product candidates, which could adversely affect our ability to generate future revenues.

Interim "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim "top-line" or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data over a longer follow-up period become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. In addition, our clinical trials have involved small patient populations; the interim results of these clinical trials may be subject to substantial variability and may not be indicative of final results. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.

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. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, the effectiveness of our patient recruitment efforts, delays in enrollment due to travel or quarantine policies, or other factors, related to COVID-19, the existing body of safety and efficacy data with respect to the study candidate, the perceived risks and benefits of gene therapy approaches for the treatment of neurological diseases, the number and nature of competing existing treatments for our target indications, the number and nature of ongoing trials for other product candidates in development for our target indications, perceived risk of the delivery procedure, patients with pre-existing conditions that preclude their participation in any trial, the proximity of patients to clinical sites and the eligibility criteria for the study. Furthermore, the negative results we have reported in clinical trials to date and any other negative results we may report in clinical trials of any of our gene therapy product candidates in the future may make it difficult or impossible to recruit and retain patients in other clinical trials of those gene therapy product candidates. Similarly, negative results reported by our competitors about their product candidates may negatively affect patient recruitment in our clinical trials. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our gene therapy product candidates or could render further development impossible. In addition, we expect to rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to control their actual performance.

We face significant competition from other biotechnology and pharmaceutical companies, 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 and our operating results will suffer if we fail to compete effectively.

Drug development, particularly in the gene therapy field, is highly competitive and subject to rapid and significant technological advancements. As a significant unmet medical need exists in the neurology field, including for the treatments of Parkinson's disease, GM1 gangliosidosis and GM2 gangliosidosis (including Tay-Sachs and Sandhoff diseases), there are several large and small pharmaceutical companies focused on delivering therapeutics for the treatment of these diseases. Further, it is likely that additional therapies will become available in the future for the treatment of our target indications.

We consider our direct competitors for AXO-AAV-GM1 or AXO-AAV-GM2 to be LYS-GM101, a gene therapy product candidate being developed by Lysogene S.A., as well as PBGM01, a gene therapy program being developed by Passage Bio which recently received IND clearance, each for the treatment of GM1 gangliosidosis, and TGTX-101, a gene therapy product candidate being developed by Taysha Gene Therapies for the treatment of GM2 gangliosidosis.

We consider our most direct competitor with respect to AXO-Lenti-PD to be Voyager Therapeutics, which previously was advancing VY-AADC, a gene therapy product candidate for the treatment of advanced Parkinson’s disease. VY-AADC delivers the AADC gene, one of the three genes contained in AXO-Lenti-PD, via an adeno-associated virus (an "AAV virus-based vector"). In May 2021, Voyager Therapeutics announced that it will not advance the VY-AADC program on its own following the termination of that portion of the collaboration agreement with Neurocrine Biosciences. Agilis Biotherapeutics, which was acquired by PTC Therapeutics, is developing AGIL-AADC, another AAV virus-based vector gene therapy that delivers the AADC gene, for the treatment of AADC deficiency, a rare disorder that involves loss of AADC gene function. In addition, DBS is approved for treating Parkinson’s disease and is marketed by multiple device manufacturers, including Medtronic, Abbott and Boston Scientific. DBS treatment involves permanent placement of hardware in the brain via stereotactic neurosurgery and may require follow-up adjustments or even invasive device replacements. Another surgical approach is Abbvie’s Duopa which is delivered via a port implanted in the abdominal wall. Further efforts are also underway to develop and commercialize new improved formulations of L-dopa, including Acorda’s Inbrija, for which an NDA was approved by the FDA in December 2018, and Mitsubishi Tanabe’s ND0612. Adjunct therapies are also being developed or have recently been approved to supplement L-dopa therapy, including Sunovion’s sublingual apomorphine and Adamas Pharmaceuticals’ GoCovri. Several companies are also trying to develop other disease modifying therapies that could prevent the progression of Parkinson’s disease. MeiraGTx is developing AAV-GAD, a gene therapy product designed to deliver the GAD gene to increase production of the neurotransmitter GABA to normalize motor circuits. Examples of early stage efforts include Denali Therapeutics’ LRRK2 inhibitors and anti-alpha synuclein antibodies from Prothena/Roche and Biogen, as well as Prevail Therapeutics’ (acquired by Eli Lilly in 2020) pipeline of AAV-based therapeutics targeting lysosomal dysfunction. BlueRock Therapeutics (acquired by Bayer in 2019) is developing an induced pluripotent stem cell-derived (iPSC) dopaminergic neuron therapy for patients with Parkinson’s and will enter a Phase 1 clinical trial in 2021 to evaluate the safety, tolerability, and preliminary efficacy in patients with Parkinson's disease.

Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, as well as in obtaining regulatory approvals of those product candidates in the United States and in foreign countries. Our current and potential future competitors also have significantly more experience commercializing drugs, particularly gene therapy and other biological products, that have been approved for marketing. Mergers and acquisitions in the pharmaceutical and biotechnology industries could result in even more resources being concentrated among a small number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer or more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomic or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

We will face competition from other drugs or from other non-drug products currently approved or that will be approved in the future in the neurology field, including for the treatment of Parkinson's disease, GM1 gangliosidosis and GM2 gangliosidosis (including Tay-Sachs and Sandhoff diseases). Therefore, our ability to compete successfully will depend largely on our ability to:

- develop and commercialize products that are superior to other products in the market;
- demonstrate through our clinical trials that our gene therapy product candidates are differentiated from existing and future therapies;
- attract qualified scientific, product development and commercial personnel;
- obtain patent or other proprietary protection for our medicines;
- obtain required regulatory approvals;
- obtain coverage and adequate reimbursement from, and negotiate competitive pricing with, third-party payors; and
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicines.

The availability of our competitors' products could limit the demand, and the price we are able to charge, for any gene therapy product candidate we develop. The inability to compete with existing or subsequently introduced products would have an adverse impact on our business, financial condition and prospects.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our gene therapy product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, discovering, developing, receiving regulatory and marketing approval for or commercializing therapies before we do, which would have an adverse impact on our business and results of operations.

If we are not able to obtain required regulatory approvals, we will not be able to commercialize our gene therapy product candidates, and our ability to generate revenue will be materially impaired.

The activities associated with the development and commercialization of our gene therapy product candidates, including their design, research, testing, manufacture, safety, efficacy, recordkeeping, labeling, packaging, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA, the PMDA and similar regulatory authorities outside the United States. Failure to obtain marketing approval for our gene therapy product candidates will prevent us from commercializing them.

We have not received approval from regulatory authorities to market any gene therapy product candidate in any jurisdiction, and we will need to complete pivotal clinical trials successfully for our gene therapy product candidates before we can submit any application for regulatory approval. It is possible that our gene therapy product candidates in the future will never obtain the appropriate regulatory approvals necessary for us to commence product sales.

We expect to rely on third-party CROs and consultants to assist us in filing and supporting the applications necessary to gain marketing approvals. Securing marketing approval requires the submission of extensive nonclinical and clinical data and supporting information for our gene therapy product candidates to regulatory authorities for each therapeutic indication to establish safety and efficacy of the gene therapy product candidate for that indication. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Delays or errors in the submission of applications for marketing approval or issues, including those related to gathering the appropriate data and the inspection process, may ultimately delay or affect our ability to obtain regulatory approval, commercialize our gene therapy product candidates and generate product revenues.

Our gene therapy product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

Adverse events caused by our gene therapy product candidates or that of adjuncts could cause us, other reviewing entities, clinical trial sites or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval. If an unacceptable frequency or severity of adverse events are reported in our clinical trials for our gene therapy product candidates or any future product candidates, our ability to obtain regulatory approval for such product candidates may be negatively impacted. The laws and regulations governing controlled substances could limit commercialization of our gene therapy product candidates, and failure to comply with those laws and regulations could also result in adverse regulatory, legal, and operational consequences.

In particular, there have been several significant adverse side effects in gene therapy treatments in the past, including reported cases of leukemia in trials using earlier generation viral vectors. Gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration which could substantially limit the effectiveness of the treatment or represent safety risks for patients. Another traditional safety concern for gene therapies using viral vectors has been the possibility of insertional mutagenesis by the vectors, leading to malignant transformation of transduced cells. Additionally, in previous clinical trials involving AAV vectors for gene therapy, some subjects experienced the development of a positive ELISPOT test associated with T-cell responses, which is of unclear clinical translatability.

There is also the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. Possible adverse side effects that may occur with treatment with gene therapy products include an immunologic reaction early after administration that could substantially limit the effectiveness of the treatment or represent safety risks for patients. Many times, side effects are only detectable after investigational products are tested in larger scale, pivotal clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval.

In addition to side effects that may be caused by gene therapy product candidates, the administration process or related procedures also can cause adverse side effects. For example, integration of AAV DNA into the host cell's genome has been reported to occur. Further, our AAV delivery systems for AXO-AAV-GM1 and AXO-AAV-GM2 have not been validated in human clinical trials previously, and if such delivery systems do not meet the safety criteria or cannot provide the desired efficacy results, then we may be forced to suspend or terminate our development of AXO-AAV-GM1 or AXO-AAV-GM2. For example, we submitted an IND in late 2019 to support the initiation of a company-sponsored clinical trial of AXO-AAV-GM2 for the treatment of patients with GM2 gangliosidosis. Following its review of the IND, while the FDA had no concerns over animal toxicology or clinical safety in the AXO-AAV-GM2 program, the FDA placed the IND on clinical hold, for which the IND was subsequently cleared in November 2020 following our responses to CMC and device-related questions. However, there can no assurance that our programs will not be subject to future clinical holds or similar delays.

If additional clinical experience indicates that any of our gene therapy product candidates has side effects or causes serious or life-threatening side effects, the development of the gene therapy product candidate may fail or be delayed, or, if the gene therapy product candidate has received regulatory approval, such approval may be revoked or limited.

Furthermore, if any of our products are approved and then cause serious or unexpected side effects, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or require a REMS to impose restrictions on its distribution or other risk management measures;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or to conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients;

- we could elect to discontinue the sale of our product; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected gene therapy product candidate and could increase the costs of commercializing our gene therapy product candidates.

Our AAV-based gene therapy product candidates and our lentiviral-based gene therapy product candidate are based on new gene transfer technology, which makes it difficult to predict the time and cost of product candidate development and of subsequently obtaining regulatory approval.

The use of gene therapy in the treatment of GM1 gangliosidosis, GM2 gangliosidosis (including Tay-Sachs disease and Sandhoff disease) and Parkinson's disease is new. We may experience problems or delays in developing new gene therapy product candidates and such problems or delays may cause unanticipated costs, and such development problems may not be solvable. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process for our gene therapy product candidates from their current manufacturers, which may prevent us from completing our clinical studies or commercializing our products on a timely or profitable basis, if at all.

In addition, the clinical trial requirements of the FDA and other foreign regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary according to the type, complexity, novelty and intended use and market of such product candidates. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied product candidates. To date, only a limited number of gene therapies have received marketing authorization from the FDA or foreign regulatory authorities. Until August 2017, the FDA had never approved a cell or gene therapy product. Since that time, it has only approved a small number of product candidates, including Kymriah by Novartis International AG, for pediatric and young adult patients with a form of acute lymphoblastic leukemia, Yescarta and Tecartus by Kite Pharma, Inc., Luxturna by Spark Therapeutics, Inc. for patients with an inherited form of vision loss, Zolgensma by Novartis International AG, for children less than 2 years old with spinal muscular atrophy, and Abecma by Bristol-Myers Squibb and bluebird bio, Inc. Additional cell and gene therapies are undergoing regulatory review in the United States and Europe. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our gene therapy product candidates in either the United States, or other major markets or how long it will take to commercialize our gene therapy product candidates, if any are approved. Approvals by foreign regulatory authorities may not be indicative of what the FDA may require for approval, and vice versa.

Regulatory requirements governing gene therapy products have changed frequently and may continue to change in the future. The FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research ("CBER") to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise the CBER in its review. If we were to engage an NIH-funded institution, to conduct a clinical trial, that institution's institutional biosafety committee as well as its IRB would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our gene therapy product candidates. Similarly, foreign regulatory authorities may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines.

The FDA, NIH and the EMA have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA advocates a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as the U.S. Congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our gene therapy product candidates.

These regulatory review committees and advisory groups and any new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions. As we advance our gene therapy product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of certain of our gene therapy product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects would be materially and adversely affected.

Even if we obtain FDA approval for our gene therapy product candidates in the United States, 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 does not ensure approval by regulatory authorities in other countries or jurisdictions. 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 costs for us and require additional nonclinical 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 obtain regulatory approval for our product candidates, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

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, the EMA, the PMDA and other comparable foreign regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and cGCP requirements for any clinical trials that we conduct post-approval. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including any requirement to implement a REMS. If any of our product candidates receives marketing approval, the accompanying labels for such products may limit the approved use of the product, which could limit sales.

Regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. For example, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The FDA typically advises that patients treated with gene therapy undergo follow-up observations for potential adverse events for a 15-year period. The holder of an approved BLA also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. These authorities closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. We will be subject to stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Prescription drugs may be promoted only for the approved indications in accordance with the approved label. 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 may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments but the FDA does restrict manufacturer's communications on the subject of off-label use of their products. Violations of the FDCA or PHSA in the United States, and other comparable regulations in foreign jurisdictions, relating to the promotion of prescription drugs may lead to enforcement actions and investigations alleging violations of U.S. federal and state health care fraud and abuse laws, as well as state consumer protection laws and comparable laws in foreign jurisdictions.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of such products;
- restrictions on product marketing, distribution or use;
- requirements to conduct post-marketing studies or clinical trials;

- warning or untitled letters;
- withdrawal of the products from the market;
- 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 such products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Government regulations may change, and additional government regulations may be enacted, either of which could prevent, limit or delay regulatory approval of our product candidates or any future product candidate. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained.

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.

Even 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, including due to the novelty of gene therapy products in general. If they do not achieve an adequate level of acceptance, we may not generate significant product revenues and become profitable. The degree of market acceptance for 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;
- the effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the ethical, social and legal concerns about gene therapy;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement and patients' willingness to pay for our products in the absence of such coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product together with other medications.

We expect sales of our product candidates, if approved, to generate substantially all of our product revenues for the foreseeable future. The failure of any of our product candidates, if approved, to find market acceptance would harm our business and could require us to seek additional financing.

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology, with only a limited number of gene therapy products approved to date. Public perception may be influenced by claims that gene therapy is unsafe, unethical or immoral, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon the comfort level of physicians to prescribe our product candidates, in lieu of, or in addition to, existing or standard treatments they are already familiar with 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 gene therapy product candidates. Earlier gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death seen in such trials using earlier generation vectors. 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. Among the risks in any gene therapy product based on viral vectors are the risks of immunogenicity, elevated liver enzymes, and insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation. If our vectors demonstrate a similar effect we may decide or be required to halt or delay further clinical development of our AAV-based product candidates. Adverse events in our clinical studies, even if not ultimately attributable to our product candidates (such as the many adverse events that typically arise from the conditioning process), or adverse events in other lentiviral gene therapy trials, and the resulting publicity, could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

Increasing demand for compassionate use or expanded access of our unapproved therapies could negatively affect our reputation and harm our business.

We are developing our product candidates for life-threatening illnesses for which there are currently limited to no available therapeutic options. It is possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide our product candidates under an expanded access corporate policy, our reputation may be negatively affected and our business may be harmed.

Recent media attention to individual patients' expanded access requests has resulted in the introduction of legislation at the local and national level referred to as "Right to Try" laws, such as the Right to Try Act, which are intended to give patients access to unapproved therapies. New and emerging legislation regarding expanded access to unapproved drugs for life-threatening illnesses could negatively impact our business in the future.

A possible consequence of both activism and legislation in this area is the need for us to initiate an unanticipated expanded access program or to make our product candidates more widely available sooner than anticipated. We are a small company with limited resources and unanticipated trials or access programs could result in diversion of resources from our primary goals.

In addition, some patients who receive access to unapproved drugs through compassionate use or expanded access programs have life-threatening illnesses and have exhausted all other available therapies. The risk for serious adverse events in this patient population is high which could have a negative impact on the safety profile of our product candidates if we were to provide them to these patients in accordance with our expanded access corporate policy, which could cause significant delays or an inability to successfully commercialize our product candidates, which could materially harm our business. If we were to provide patients with our product candidates under an expanded access program, we may in the future need to restructure or pause ongoing compassionate use and/or expanded access programs in order to perform the controlled clinical trials required for regulatory approval and successful commercialization of our product candidates, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs.

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, even if approved.

We do not have an infrastructure for the sales, marketing or distribution of our product candidates should they be approved, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any product that may be approved, we must build our sales, distribution, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services and obtain requisite licenses. To achieve commercial success for any product for which we have obtained marketing approval, we will need a sales and marketing organization.

We plan to commercialize our product candidates in the United States, the EU, Japan and other major markets. If our product candidates are approved for marketing, we may build a focused sales, distribution and marketing infrastructure to market them. There are significant expenses and risks involved with establishing our own sales, marketing and distribution capabilities, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities, and any failure to obtain and maintain the requisite licenses, could delay any product launch, which would adversely impact the commercialization of our product candidates.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or attain adequate numbers of physicians to prescribe any drugs;
- the inability to negotiate with payors regarding reimbursement for our products; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to build our own sales force or negotiate a collaborative relationship for the commercialization of our product candidates, we may be forced to delay the potential commercialization of such products or reduce the scope of our sales or marketing activities for our product candidates. If we elect to increase our expenditures to fund commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring our product candidates to market or generate product revenue. We could enter into arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to one or more of our product candidates or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business, operating results and prospects.

If the market opportunities for any product candidates we may develop are smaller than we believe they are, our revenues, if any, may be adversely affected, and our business may suffer. Because the target patient populations for many of the product candidates we may develop are small, we must be able to successfully identify patients and achieve a significant market share to achieve and maintain profitability and growth.

We focus our research and product development on treatments for diseases with limited or no therapeutic options. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with product candidates we may develop, are based on estimates. These estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe and elsewhere may turn out to be lower than expected, and patients may not be amenable to treatment with our products, or may become increasingly difficult to identify or gain access to, all of which could harm our business, financial condition, results of operations, and prospects.

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

- If our product candidates are approved for commercialization, we may enter into agreements with third parties to market them in certain jurisdictions outside the United States. We expect that we will be subject to additional risks related to international operations or entering into international business relationships, including:
- different regulatory requirements for drug approvals and rules governing drug commercialization in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign reimbursement, pricing and insurance regimes;
- foreign taxes;

- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act and similar anti-bribery and anti-corruption laws in other jurisdictions;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

Our current and future relationships with investigators, health care professionals, consultants, third-party payors, 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 and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations.

These laws may regulate the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our products for which we obtain marketing approval. Such laws include:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, 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 a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation; in addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the federal false claims laws including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, and civil monetary penalties laws, which impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented to the federal government, claims for payment 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 knowingly making, or causing to be made, a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; in addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- HIPAA imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false or fraudulent statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information on health plans, health care clearing houses, and certain health care providers, known as covered entities, and their business associates, defined as independent contractors or agents of covered entities that create, receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity as well as their covered subcontractors;
- a number of federal, state and foreign laws, regulations, guidance and standards that impose requirements regarding the protection of health data that are applicable to or affect our operations;

- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report such information regarding their relationships with physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and certified nurse midwives during the previous year; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, 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 non-governmental third-party payors, including private insurers, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing, as well as state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our current and future business arrangements with third parties will 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 healthcare laws. If our operations are found to be in violation of any of these or any other health regulatory laws that may apply to us, we may be subject to significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Even the mere issuance of a subpoena or the fact of an investigation alone, regardless of the merit, may result in negative publicity, a drop in our stock price, and other harm to our business, financial condition and results of operations.

Defending against any such actions can be costly, time-consuming and may require significant financial and 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.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "Affordable Care Act") was enacted to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The law has continued the downward pressure on pharmaceutical pricing, especially under the Medicare program, and increased the industry's regulatory burdens and operating costs. Among the provisions of the Affordable Care Act of importance to our product candidates are the following:

- an annual, nondeductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;

- 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;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer point-of-sale discounts of 70% off negotiated prices of applicable brand drugs to eligible beneficiaries under their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs in certain states;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a licensure framework for follow on biologic products;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There remain judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as efforts by the current administration to repeal or replace certain aspects of the Affordable Care Act. Since January 2017, the President of the United States has signed Executive Orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act of 2017, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act's "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax.

Further, the Bipartisan Budget Act of 2018, among other things, amended the Affordable Care Act, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In addition, the federal government eliminated federal cost-sharing reduction ("CSR") payments to insurance companies. The loss of such federal CSR payments has resulted in increased premiums on certain policies issued by qualified health plans under the Affordable Care Act. Moreover, in December 2018, the Centers for Medicare & Medicaid Services ("CMS") published a new final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On April 27, 2020, the United States Supreme Court reversed a Federal Circuit decision that previously upheld Congress' denial of $12 billion in "risk corridor" funding. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act of 2017, the remaining provisions of the Affordable Care Act are invalid as well. In December 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case. It is unclear how such litigation and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act and our business. The Affordable Care Act is likely to continue the downward pressure on pharmaceutical pricing and may also increase our regulatory burdens and operating costs. We continue to evaluate the effect that the Affordable Care Act and its possible repeal and replacement has on our business.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This included further reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2030 unless additional Congressional action is taken. The Coronavirus Aid, Relief and Economic Security Act, or CARES Act, which was signed into law in March 2020 and is designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030. Additionally, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period in which the government may recover overpayments to providers from three to five years.

Further, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the out-of-pocket cost of prescription drugs and reform government program reimbursement methodologies for drugs. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to pharmaceutical product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the current administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the U.S. presidential administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases.

Additionally, on May 11, 2018, the President of the United States previously laid out his administration's "Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs" to reduce the cost of prescription drugs while preserving innovation and cures. The Department of Health and Human Services has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. Congress and the U.S. presidential administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Additionally, on July 24, 2020, President Trump announced four executive orders related to prescription drug pricing that attempt to implement several of the Trump administration proposals, including (i) a policy that would tie certain Medicare Part B drug prices to international drug prices, or the "most favored nation price," the details of which were released on September 13, 2020 and also expanded the policy to cover certain Part D drugs; (ii) an order that directs HHS to finalize the Canadian drug importation proposed rule previously issued by HHS and makes other changes allowing for personal importation of drugs from Canada; (iii) an order that directs HHS to finalize the rulemaking process on modifying the Anti-Kickback Statute safe harbors for discounts for plans, pharmacies, and pharmaceutical benefit managers; (iv) a policy that reduces costs of insulin and epipens to patients of federally qualified health centers. The FDA also recently released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, whether the current regulations, guidance or interpretations will be changed, or what the impact of such changes on our business, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. In addition, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

Coverage and adequate reimbursement may not be available for our product candidates, which could make it difficult for us to sell our products profitably, if approved.

Market acceptance and sales of any approved product candidates that we develop will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government health administration authorities and private health insurers. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Third-party payors decide which drugs or therapies they will pay for and establish reimbursement levels. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage, and adequate reimbursement, for the product. Additionally, a third-party payor's decision to provide coverage for a drug or therapy does not imply that an adequate reimbursement rate will be approved. Each plan determines whether or not it will provide coverage for a drug or therapy, what amount it will pay the manufacturer for the drug or therapy, on what tier of its formulary the drug or therapy will be placed, and whether to require step therapy. The position of a drug on a formulary generally determines the co-payment that a patient will need to make to obtain the drug and can strongly influence the adoption of a drug by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost of our products.

The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Even if we do obtain adequate levels of reimbursement, third-party payors, such as government or private healthcare insurers, carefully review and increasingly question the coverage of, and challenge the prices charged for, products. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Increasingly, third-party payors are requiring that pharmaceutical companies provide them with predetermined discounts from list prices and are challenging the prices charged for products. We may also be required to conduct expensive pharmacoeconomic studies to justify the coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage or reimbursement may impact the demand for, or the price of, any product for which we obtain marketing approval. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize any product candidates that we develop.

Additionally, there have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell any future drugs profitably. There can be no assurance that our product candidates, if approved, will be considered medically reasonable and necessary, that it will be considered cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available, or that reimbursement policies and practices in the United States and in foreign countries where our products are sold will not adversely affect our ability to sell our product candidate profitably, if approved for sale.

Risks Related to Our Dependence on Third Parties

Gene therapies are novel, complex, difficult and expensive to manufacture. We do not have our own manufacturing capabilities and will rely on third parties to produce clinical and commercial supplies of our product candidates.

We are building teams with drug formulation and manufacturing expertise but do not own or operate, nor do we expect to own or operate in the foreseeable future, facilities for product manufacturing, storage and distribution, or testing. In addition to the technical challenges of drug product formulation and scale-up and environmental compliance aspects of chemical and biologics manufacturing, our vendors of manufacturing services will need to comply with U.S. and foreign regulatory authority licensure and cGMP quality requirements. These obligations are enforced by periodic inspection and audit by regulatory authorities, and any adverse findings or violations discovered on such inspections could distract our vendors and be costly and time consuming to remediate, potentially impacting their supply of clinical and future commercial products to us.

Under the Oxford Agreement, Oxford will manufacture and supply the AXO-Lenti-PD in accordance with separate clinical and commercial supply agreements, which will be negotiated between us and Oxford. The Oxford Agreement contains certain key provisions of the clinical and commercial supply agreements, including pricing structure and our ability to transfer the technology to another manufacturer at any time following the completion of formal process characterization, process validation or BLA submission. In July 2020, we entered into an agreement with Viralgen Vector Core, S.L. for the manufacture of all additional clinical trial material for our AXO-AAV-GM1 and AXO-AAV-GM2 development programs and subsequent commercial supply.

Our reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including:

- failure to satisfy their contractual duties or obligations;
- inability to meet our product specifications and quality requirements consistently;
- delay or inability to develop, procure or expand sufficient manufacturing capacity;
- manufacturing and/or product quality issues related to manufacturing development and scale-up;
- costs and validation of new equipment and facilities required for scale-up;
- failure to comply with applicable laws, regulations, and standards, including cGMP and similar foreign standards;
- deficient or improper record-keeping;
- contractual restrictions on our ability to engage additional or alternative manufacturers;
- inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our product candidates or any future product candidate in a timely fashion, in sufficient quantities or under acceptable terms;
- lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;
- lack of access or licenses to proprietary manufacturing methods used by third-party manufacturers to make our product candidates;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or regulatory sanctions related to the manufacture of our or other company's products;
- carrier disruptions or increased costs that are beyond our control; and
- failure to deliver our products under specified storage conditions and in a timely manner.

The process for manufacturing gene therapy products, including our product candidates, is more complex than those required for most chemical pharmaceuticals, requiring substantial expertise, specialized facilities, highly specific raw materials and significant capital investment and involving other production constraints. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a gene therapy product such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner or that the dosing will be uniform in our products. Accordingly, we and our manufacturers employ multiple steps to control our manufacturing process to assure that the process works and that our product candidates are made strictly and consistently in compliance with the process. Problems with the manufacturing process, including even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade or commercial-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs. In addition, the FDA, EMA and other regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, EMA or other regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Delays in manufacturing processes at our third party manufacturers, including recently at Oxford, which may be outside of our control, have resulted in, and may in the future result in, delays in our planned clinical trials. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

Due to the complexity and constraints associated with manufacturing gene therapy products, there is a limited number of suppliers that can adequately and timely provide the raw materials, including vectors, for our product candidates, particularly if we commence larger clinical trials and studies for our product candidates. If supply from a manufacturing facility is interrupted, including due to equipment malfunctions, facility contamination, material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of suppliers, there could be a significant disruption in supply of our product candidates. We have also terminated supply and manufacturing agreements in the past, and may terminate such agreements in the future, which could also result in supply disruptions. If we are unable to engage other manufacturers or suppliers, we may not be able to enter into arrangements with them on favorable terms or at all. Use of new third-party manufacturers could increase the risk of delays in production or insufficient supplies of our product candidates as we transfer our manufacturing technology to these manufacturers and as they gain experience manufacturing our product candidates. Further, due to intense competition among companies developing gene therapy product candidates, we may encounter difficulties in sourcing adequate supply for our gene therapy products on a timely or cost-efficient basis.

We have no experience manufacturing any of our product candidates. Building our own manufacturing facility, if we decide to do so in the future, would require substantial additional investment, would be time-consuming and may be subject to delays, including those resulting from compliance with regulatory requirements. We also may encounter problems hiring and retaining the experienced specialist scientific, quality control and manufacturing personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. Although we may establish our own manufacturing facility or use that of a third-party contract manufacturer to support a commercial launch of our gene therapy product candidates, if approved, the timeframe for us to obtain approval for such facility or qualify such third-party contract manufacturer and ensure that all processes, methods and equipment are compliant with cGMP requirements is uncertain. We must supply all necessary documentation in support of a BLA or other MAA on a timely basis and must adhere to the FDA's and EMA's cGMP requirements before any of our product candidates can obtain marketing approval. To date, to our knowledge, a limited number of cGMP gene therapy manufacturing facilities have received approval from the FDA for the manufacture of an approved gene therapy product and, therefore, the timeframe required for us to obtain such approval is uncertain. We are subject to audits from FDA, EMA and other authorities that may result in observations of non-compliance from cGMP requirements. In addition, our ability to receive damages from our CROs in connection with such failures is generally contractually limited.

Any of these events affecting our product candidates or those of adjuncts could lead to clinical trial delays, cost overruns, delay or failure to obtain regulatory approval or impact our ability to successfully commercialize our products, as well as potential product liability litigation, product recalls or product withdrawals. Some of these events could be the basis for FDA action, including injunction, recall, seizure, or total or partial suspension of production.

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

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

We intend to rely on third parties to conduct, supervise and monitor our nonclinical studies and our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We intend to rely on CROs and nonclinical and clinical trial sites to ensure the proper and timely conduct of our nonclinical studies and our clinical trials, and we expect to have limited influence over their actual performance. In addition, pursuant to our agreements with UMMS and Oxford, we may rely on their respective employees for certain services in connection with the transition of the respective gene therapy product candidates to us. We do not have complete control over those employees or their execution of services provided to us, and those employees may not perform such services in a timely or satisfactory manner, which could harm our business and development programs.

We intend to rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future nonclinical studies. We expect to control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs will be required to comply with Good Laboratory Practices ("GLPs") and cGCPs, which are regulations and guidelines enforced by the FDA and are also required by the competent authorities of the member states of the European Economic Area and comparable foreign regulatory authorities in the form of International Council for Harmonization guidelines for any of our product candidates that are in nonclinical and clinical development. The regulatory authorities enforce cGCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. Although we may rely on CROs to conduct our GLP-compliant preclinical studies and GCP-compliant clinical trials, we will remain responsible for ensuring that each of our GLP preclinical studies and GCP clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. If we or our CROs fail to comply with cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may reject our marketing applications or require us to perform additional clinical trials before approving our marketing applications. Accordingly, if we or our CROs fail to comply with these regulations or other applicable laws, regulations or standards, or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the relevant regulatory approval process. Failure by our CROs to properly execute study protocols in accordance with applicable law could also create product liability and healthcare regulatory risks for us as sponsors of those studies.

Our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs 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 which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret and intellectual property protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our (or their own) clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop could be harmed, our costs could increase, and our ability to generate revenues could be delayed.

If our relationships with these CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms or in a timely manner. 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.

We may seek to enter into collaborations in the future with other third parties. If we are unable to enter into such collaborations, or if these collaborations are not successful, our business could be adversely affected.

We will seek to enter into additional collaborations in the future, including sales, marketing, distribution, development, licensing, and/or broader collaboration agreements. Our likely collaborators include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies, and medical device manufacturers. However, we may not be able to enter into additional collaborations on favorable terms or at all. Our ability to generate revenues from our collaborations will depend on our and our collaborators' abilities to successfully perform the functions assigned to each of us in these arrangements. In addition, our collaborators have the ability to abandon research or development projects and terminate applicable agreements. Moreover, an unsuccessful outcome in any clinical trial for which our collaborator is responsible could be harmful to the public perception and prospects of our existing product candidate pipeline.

Our relationship with any future collaborations may pose several risks, including the following:

- collaborators have significant discretion in determining the amount and timing of the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- the nonclinical studies and clinical trials conducted as part of these collaborations may not be successful;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on nonclinical study or clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;

- collaborators may delay nonclinical studies and clinical trials, provide insufficient funding for nonclinical studies and clinical trials, stop a nonclinical study or clinical trial or abandon a product candidate, repeat or conduct new nonclinical studies or clinical trials or require a new formulation of a product candidate for nonclinical studies or clinical trials;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates developed in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development of any product candidates, may cause delays or termination of the research, development or commercialization of such product candidates, may lead to additional responsibilities for us with respect to such product candidates or may result in litigation or arbitration, any of which would be time consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- disputes may arise with respect to the ownership or inventorship of intellectual property developed pursuant to our collaborations;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- the terms of our collaboration agreement may restrict us from entering into certain relationships with other third parties, thereby limiting our options; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

We will face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement with any future collaborators will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of several factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators.

Risks Related to Our Common Stock

An active trading market for our common stock may not be sustained.

Although our common stock is listed on the Nasdaq Global Select Market ("Nasdaq"), we cannot assure you that an active trading market for our common stock will be sustained. In addition, as a result of Roivant Sciences Ltd. ("RSL") owning approximately 26.8% of our shares of common stock outstanding as of March 31, 2021, trading in our common stock may be less liquid than the stock of companies with broader public ownership. If an active market for our common stock is not sustained, you may not be able to sell your stock quickly or at the market price. An inactive market may also impair our ability to raise capital to continue to fund operations by selling shares of our common stock and may impair our ability to acquire other companies or technologies by using our common stock as consideration.

The market price of our common stock has been and is likely to continue to be highly volatile, and you may lose some or all of your investment.

The market price of our common stock has been and is likely to continue to be highly volatile and may be subject to wide fluctuations in response to a variety of factors, including the following:

- any additional delays in the commencement, enrollment and ultimate completion of our clinical trials, including as a result of the clinical hold placed on our AXO-AAV-GM2 program that was lifted in November 2020, and manufacturing delays for our AXO-Lenti-PD program;
- results of clinical trials of our product candidates or those of our competitors;
- any delay in filing applications for marketing approval of our product candidates, and any adverse development or perceived adverse development with respect to applicable regulatory authorities' review of those applications;
- failure to successfully develop and commercialize our product candidates;
- failure to maintain our relationship with Oxford or UMMS or comply with the terms of the Oxford Agreement or the UMMS Agreement;
- inability to obtain additional funding;
- inability to obtain, protect or maintain necessary intellectual property;
- regulatory or legal developments in the United States and other countries applicable to our product candidates, including gene therapies;
- adverse regulatory decisions or statements;
- changes in the structure of healthcare payment systems;
- inability to obtain adequate product supply for our current product candidates or any future product candidate, or the inability to do so at acceptable prices;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- changes in the market valuations of similar companies;
- market conditions in the pharmaceutical and biotechnology sectors, and the issuance of new or changed securities analysts' reports or recommendations;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- significant lawsuits, including patent or stockholder litigation, and disputes or other developments relating to our proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- short sales of our common stock;
- sales of shares of our common stock by us or our stockholders in the future;
- negative coverage in the media or analyst reports, whether accurate or not;
- issuance of subpoenas or investigative demands, or the public fact of an investigation by a government agency, whether meritorious or not;
- trading volume of our common stock;
- general economic, industry and market conditions; and

- the other factors described in this "Risk Factors" section.

In addition, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies, including in connection with the ongoing COVID-19 pandemic, which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. These fluctuations have often been unrelated or disproportionate to the operating performance of those companies. Broad market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to the ongoing COVID-19 pandemic, as well as general economic, political, regulatory and market conditions, may negatively affect the market price of our common stock, regardless of our actual operating performance.

Volatility in our stock price could subject us to securities class action litigation.

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

RSL owns a significant percentage of our shares of common stock and is able to exert significant control over matters subject to stockholder approval.

Based on shares of our common stock outstanding as of March 31, 2021, RSL beneficially owns approximately 26.8% of the voting power of our outstanding shares of common stock and has the ability to substantially influence us through this ownership position. RSL's interests may not always coincide with our corporate interests or the interests of other stockholders, and RSL may act in a manner with which you may not agree or that may not be in the best interests of our other stockholders. In 2020, RSL closed a transaction with Sumitomo Dainippon Pharma Co., Ltd. ("Sumitomo") that includes a grant to Sumitomo of a right of first refusal with respect to our shares of common stock held by RSL, which could result in RSL taking actions that may not coincide with our corporate interests or the interests of other stockholders, and could impact our ability to undertake certain corporate transactions. Further, RSL is a privately held company whose ownership and governance structure is not transparent to our other stockholders. RSL recently entered into a business combination agreement with Montes Archimedes Acquisition Corp., a special purpose acquisition corporation, pursuant to which RSL would become a publicly-traded corporation if such transaction is completed. There may be changes to the management or ownership of RSL that could impact RSL's interests in a way that may not coincide with our corporate interests or the interests of other stockholders. So long as RSL continues to own a significant amount of our equity, RSL will continue to be able to strongly influence our decisions.

Our organizational and ownership structure may create significant conflicts of interests.

Our organizational and ownership structure involves a number of relationships that may give rise to certain conflicts of interest between us and minority holders of our common stock, on the one hand, and RSL and its shareholders, on the other hand. Certain of our directors and employees have equity interests in RSL and, accordingly, their interests may be aligned with RSL's interests, which may not always coincide with our corporate interests or the interests of our other stockholders. Further, our other stockholders may not have visibility into the RSL ownership of any of our directors or officers, which may change at any time through acquisition, disposition, dilution, or otherwise. Any change in our directors' or officers' RSL ownership could impact the interests of those holders.

In addition, we are party to certain related party agreements with RSL and its wholly owned subsidiaries, Roivant Sciences, Inc. ("RSI") and Roivant Sciences GmbH ("RSG"). These entities and their shareholders, including certain of our directors and employees, may have interests which differ from our interests or those of the minority holders of our common stock. For example, we are party to an information sharing and cooperation agreement with RSL pursuant to which RSL has granted us a right of first review on any potential dementia-related product or investment opportunity that RSL may consider pursuing. It is possible that we could fail to pursue a product candidate under this agreement and that product candidate is then successfully developed and commercialized by RSL or one of its other subsidiaries or affiliates. Any material transaction between us and RSL, RSI or RSG is subject to our related party transaction policy, which requires prior approval of such transaction by our Audit Committee. To the extent we fail to appropriately deal with any such conflicts of interests, it could negatively impact our reputation and ability to raise additional funds and the willingness of counterparties to do business with us, all of which could have an adverse effect on our business, financial condition, results of operations and cash flows.

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

We have never declared or paid any cash dividends on shares of our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock would be your sole source of gain on an investment in our common stock for the foreseeable future.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change of control was considered favorable by you and other stockholders. For example, our board of directors will have the authority to issue up to 10,000,000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change of control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents will also contain other provisions that could have an anti-takeover effect, including:

- stockholders will not be entitled to remove directors other than by a 66 2/3% vote and only for cause;
- stockholders cannot call a special meeting of stockholders;
- stockholders cannot act by written consent in lieu of a meeting; and
- stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change of control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Our certificate of incorporation and bylaws provide that the Court of Chancery of the State of Delaware or, under certain circumstances, the federal district courts of the United States of America are the exclusive forums for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.

Our certificate of incorporation and bylaws provide that the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, any state court located within the State of Delaware or, if all such state courts lack subject matter jurisdiction, the federal district court for the District of Delaware) is the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;
- any action arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation, or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

These provisions would not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended (the "Exchange Act") or any claim for which the federal district courts of the United States of America have exclusive jurisdiction. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims.

Our stockholders cannot waive compliance with the federal securities laws and the rules and regulations thereunder. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of, and consented to, the provisions of our amended and restated certificate of incorporation described in the preceding sentences.

To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our certificate of incorporation and bylaws further provide that the federal district courts of the United States are the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our certificate of incorporation and bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find the exclusive-forum provisions in our amended and restated certificate of incorporation to be inapplicable or unenforceable, we may incur additional costs associated with resolving the dispute in other jurisdictions.

Your rights as a stockholder arise under Delaware law as well as our Delaware certificate of incorporation and bylaws.

The rights of our stockholders arise under our certificate of incorporation and bylaws as well as Delaware law. These organizational documents and Delaware law contain provisions for class actions and derivative actions, which may result in becoming involved in costly litigation, which could harm our business. In addition, our bylaws may generally be amended by our board of directors, as permitted under the provisions of Section 203 of the Delaware General Corporation Law ("DGCL"). Additionally, while the provisions of Section 203 of the DGCL regarding business combination provisions currently apply, there can be no assurance that the rights afforded by Section 203 of the DGCL will not be changed or rescinded by the Delaware legislature or courts in the future.

Future sales of shares of our common stock, or the perception that such sales may occur, could depress our stock price, even if our business is doing well.

As of March 31, 2021, 18,577,380 of our outstanding shares of common stock, representing 26.8% of our shares of common stock, were held by RSL. If RSL, or any of our executive officers or directors, were to sell our common stock, or if the market perceived that RSL or any of our executive officers or directors intend to sell our common stock, it could negatively affect our stock price. Such a decrease in our stock price could also in turn impair our ability to raise capital through the sale of additional equity securities.

Further, we have filed registration statements on Form S-8 under the Securities Act to register the common stock that may be issued under our equity incentive plans from time to time. Stock registered under these registration statements is available for sale in the public market subject to vesting arrangements and exercise of options, as well as Rule 144 in the case of our affiliates. Sales of these shares of common stock may negatively impact our stock price.

In addition, we have filed a "shelf" registration statement on Form S-3 under the Securities Act, allowing us, from time to time, to offer up to $750 million of any combination of registered shares of common stock or preferred stock, debt securities and warrants. We have also entered into a sales agreement with SVB Leerink LLC to sell shares of common stock from time to time through an at-the-market equity offering program with an aggregate offering price of up to approximately $36.3 million remaining available to be sold as of June 8, 2021. To the extent we issue new shares of common stock as a result of needing additional capital, such stock could constitute a material portion of our then outstanding shares of common stock and cause dilution to our existing stockholders.

If we are unable to maintain proper and effective internal controls over financial reporting and disclosure controls and procedures, investor confidence in our company and, as a result, the value of our common stock, may be adversely affected.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and to protect from fraudulent, illegal or unauthorized transactions. Effective disclosure controls and procedures enable us to make timely and accurate disclosure of financial and non-financial information that we are required to disclose. If we cannot provide effective controls and reliable financial reports and other disclosures, our business and operating results could be harmed. We have in the past discovered, and may in the future discover, areas of our internal controls over financial reporting or disclosure controls and procedures that, even if effective, could be improved.

We are required, pursuant to Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on the effectiveness of our internal control over financial reporting as of the end of each fiscal year. Our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting until our first annual report required to be filed with the SEC following the date we are deemed to be an "accelerated filer," as defined in the Exchange Act.

If material weaknesses or control deficiencies occur or our disclosure controls and procedures are ineffective in the future, we may be unable to report our financial results or make other disclosures accurately on a timely basis, which could cause our reported financial results or other disclosures to be materially misstated and result in the loss of investor confidence and cause the market price of our common stock to decline.

We are a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to smaller reporting companies will make our common stock less attractive to investors.

We currently qualify as a "smaller reporting company". For so long as we continue to be a smaller reporting company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not smaller reporting companies, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and we also may still qualify as a "non-accelerated filer" which provides for exemption from compliance with the auditor attestation requirements of Section 404.

We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

The change of our jurisdiction of incorporation from Bermuda to Delaware on November 12, 2020 (the "Domestication") may result in adverse tax consequences for holders of our common shares prior to the Domestication.

As discussed more fully under “Material U.S. Federal Income Tax Consequences of the Domestication” included as Exhibit 99.1 to our Current Report on Form 8-K12G3, filed November 13, 2020 (the "Current Report"), we believe that the Domestication constituted a tax-free reorganization within the meaning of Section 368(a)(l)(F) of the Code. Assuming the Domestication so qualifies, U.S. holders (as defined in “Material U.S. Federal Income Tax Consequences of the Domestication” in the S-4 Registration Statement) of Sio Gene Therapies Inc. (formerly Axovant Gene Therapies Ltd. until the Domestication became effective) ("Sio") common shares or warrants are subject to Section 367(b) of the Code and, as a result, such U.S. holders may be subject to U.S. federal income tax as a result of the Domestication depending on their status. Although it is not entirely free from doubt, because the warrants are pre-funded warrants, we believe the warrants should be treated as Sio common shares for U.S. federal income tax purposes and a holder of warrants should generally be taxed in the same manner as a holder of Sio common shares, as described below. The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes and all references to Sio common shares include warrants (including with respect to the determination of percentage ownership of a holder).

If you are a U.S. holder who owned Sio common shares that had a fair market value of less than $50,000 at the time the Domestication occurred, you generally will not recognize any gain or loss and will not be required to include any part of Sio’s earnings in income.

If you are a U.S. holder who owned Sio common shares that had a fair market value of $50,000 or more, but less than 10% (actually or constructively) of (i) the total combined voting power of all classes of our shares entitled to vote at general meetings of Sio on the day of Domestication occurred and (ii) the total value of all classes of our shares at the time the Domestication occurred, then except as noted below, you must generally recognize gain (but not loss) with respect to such common stock of Sio received in the Domestication, even if you continue to hold your stock and have not received any cash as a result of the Domestication. As an alternative to recognizing gain, however, such U.S. holder may elect to include in income the "all earnings and profits amount," as the term is defined in Treasury Regulation Section 1.367(b)-2(d), attributable to its common shares in Sio provided certain other requirements are satisfied. The income so included pursuant to this election generally would be treated as dividend income. Notwithstanding the foregoing, however, we, in consultation with our tax advisor, believe that Sio's cumulative earnings and profits were not greater than zero through the day of the Domestication. Each shareholder should get their own tax advice, however it is expected that on this basis, the making of an election to include the person's share of the "all earnings and profits amount" into income as a dividend generally would not be expected to result in an adverse effect to U.S. holders who would otherwise recognize gain with respect to the conversion of the Axovant Gene Therapies Ltd. common shares in the Domestication. **THE TAX CONSEQUENCES OF THE DOMESTICATION ARE COMPLEX AND DEPEND ON A HOLDER'S PARTICULAR CIRCUMSTANCES. WE STRONGLY URGE EACH SUCH U.S. HOLDER TO READ CAREFULLY OUR DESCRIPTIONS OF THE ELECTION IN "MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES OF THE DOMESTICATION" IN THE CURRENT REPORT, AS WELL AS TO CONSULT ITS OWN TAX ADVISOR FOR A FULL DESCRIPTION OF THE TAX CONSEQUENCES OF THE DOMESTICATION, INCLUDING THE APPLICABILITY AND EFFECT OF U.S. FEDERAL, STATE, LOCAL AND NON-U.S. INCOME AND OTHER TAX LAWS.**

If a U.S. holder owned Sio common shares with 10% (actually or constructively) or more of the total combined voting power of all classes of our shares entitled to vote at general meetings of Sio on the day the Domestication occurred or 10% or more of the total value of all classes of our shares at the time the Domestication occurred, such U.S. holder will generally be required to pay taxes on a deemed dividend equal to the "all earnings and profits amount" attributable to its common shares in Sio. As noted above, we, in consultation with our tax advisor, believe that Sio's cumulative earnings and profits were not greater than zero through the day of the Domestication. Complex attribution rules apply in determining whether a U.S. holder owns 10% or more of the total combined voting power of all classes of our shares for U.S. federal tax purposes. **EACH U.S. HOLDER IS STRONGLY URGED TO CONSULT ITS OWN TAX ADVISOR.**

If we are (or were at any time during such U.S. holder's holding period) characterized as a passive foreign investment company ("PFIC"), U.S. holders of our common shares may have suffered adverse tax consequences in connection with the Domestication. In addition, special information reporting may be required. We do not believe that we were (for our taxable year ending on the date of the Domestication), or have been, characterized as a PFIC; however, there can be no assurance that the IRS will agree with our conclusion and that the IRS would not successfully challenge our position. See "Material U.S. Federal Income Tax Consequences of the Domestication" in the S-4 Registration Statement.

If you are a non-U.S. holder (as defined in "Material U.S. Federal Income Tax Consequences of the Domestication" in the Current Report) of our common shares or warrants, you may be subject to withholding tax on any dividends paid on the shares of common stock of Sio subsequent to the Effective Time. Please read the following information which provides more details on the potential tax consequences of the Domestication.

For a more detailed description of the material U.S. federal income tax consequences associated with the Domestication, please read "Material U.S. Federal Income Tax Consequences of the Domestication" in the S- 4 Registration Statement. **THE TAX CONSEQUENCES OF THE DOMESTICATION ARE COMPLEX AND WILL DEPEND ON A HOLDER'S PARTICULAR CIRCUMSTANCES. WE STRONGLY URGE YOU TO CONSULT WITH YOUR OWN TAX ADVISOR FOR A FULL DESCRIPTION OF THE TAX CONSEQUENCES OF THE DOMESTICATION, INCLUDING THE APPLICABILITY AND EFFECT OF U.S. FEDERAL, STATE, LOCAL AND NON-U.S. INCOME AND OTHER TAX LAWS.**

The intended tax effects of our corporate structure prior to and following the Domestication and our corporate reorganization to align our corporate structure with current and future business activity (the "Reorganization"), and intercompany arrangements prior to the Domestication and Reorganization, depend on the application of the tax laws of various jurisdictions and on how we operate our business.

The Domestication and Reorganization involved the tax authorities and related rules and regulations of multiple international jurisdictions. In connection with the Domestication and Reorganization, we relied on the availability of certain exemptions from tax, and losses and other deductions, in certain such jurisdictions in respect of steps being taken as part of the Domestication and Reorganization, which are complex. If the tax authorities of any such jurisdictions do not agree with such exemptions, losses or deductions, we may be subject to tax charges and liabilities. Following the Domestication and Reorganization, we still have subsidiaries that are domiciled in the U.K., Switzerland and Ireland. Our corporate structure is organized so that we can achieve our business objectives in a tax-efficient manner following the Domestication and Reorganization and control operating expenses. Historically, we have conducted operations prior to the Domestication and Reorganization through subsidiaries in various countries and tax jurisdictions, including the U.K. and Switzerland, in part through intercompany service agreements between RSL and certain of its subsidiaries, our subsidiaries and us. In that case, our corporate structure and intercompany transactions, including the manner in which we developed and used our intellectual property, were organized to achieve our business objectives in a tax-efficient manner and in compliance with applicable transfer pricing rules and regulations. If two or more affiliated companies are located in different countries or tax jurisdictions, the tax laws and regulations of each country generally will require that transfer prices be the same as those between unrelated companies dealing at arms' length and that appropriate documentation be maintained to support the transfer prices. While we believe that we have operated in compliance with applicable transfer pricing laws, our transfer pricing procedures are not binding on applicable tax authorities. If tax authorities in any of these countries were to successfully challenge our transfer prices as not reflecting arms' length transactions in historical periods prior to the Domestication and Reorganization, they could require us to adjust our transfer prices and thereby reallocate our income to reflect these revised transfer prices, which could result in a higher tax liability to us. In addition, if the country from which the income is reallocated does not agree with the reallocation, both countries could tax the same income, potentially resulting in double taxation. If tax authorities were to allocate income to a higher tax jurisdiction, subject our income to double taxation or assess interest and penalties, it would increase our consolidated tax liability, which could adversely affect our financial condition, results of operations and cash flows.

Judgment is required in evaluating our tax positions and determining our provision for income taxes. During the ordinary course of business, there are many transactions and calculations for which the ultimate tax determination is uncertain. For example, our effective tax rates could be adversely affected by changes in foreign currency exchange rates or by changes in the relevant tax, accounting, and other laws, regulations, principles, and interpretations. As we intend to operate in more than one country and taxing jurisdiction, the application of tax laws can be subject to diverging and sometimes conflicting interpretations by tax authorities of these jurisdictions. It is not uncommon for taxing authorities in different countries to have conflicting views, for instance, with respect to, among other things, the manner in which the arm's length standard is applied for transfer pricing purposes, or with respect to the valuation of intellectual property. In addition, tax laws are dynamic and subject to change as new laws are passed and new interpretations of the law are issued or applied. Moreover, certain relevant tax, accounting and other laws have special application with respect to "affiliated," "combined" or similar groups, which included RSL and its subsidiaries prior to March 2020, and which may impact the tax liabilities of the companies. We continue to assess the impact of such changes in tax laws on our business and may determine that changes to our structure, practice or tax positions are necessary in light of such changes and developments in the tax laws of other jurisdictions in which we operate. Such changes may nevertheless be ineffective in avoiding an increase in our consolidated tax liability, which could harm our financial condition, results of operations and cash flows.

Changes in our effective tax rate may reduce our net income in future periods.

Our tax position could be adversely impacted by changes in tax rates, tax laws, tax practice, tax treaties or tax regulations or changes in the interpretation thereof by the tax authorities in Ireland, the United States and other jurisdictions for periods following the Domestication and Reorganization, and also Europe (including the U.K. and Ireland), the United States and other jurisdictions for historical periods prior to the Domestication and Reorganization. Such changes may become more likely as a result of recent economic trends in the jurisdictions in which we operate, particularly if such trends continue. If such a situation was to arise, it could adversely impact our tax position and our effective tax rate. Failure to manage the risks associated with such changes, or misinterpretation of the laws providing such changes, could result in costly audits, interest, penalties and reputational damage, which could adversely affect our business, results of our operations and our financial condition.

Our actual effective tax rate may vary from our expectation and that variance may be material. A number of factors may increase our future effective tax rates, including: (1) the jurisdictions in which profits are determined to be earned and taxed; (2) the resolution of issues arising from any future tax audits with various tax authorities; (3) changes in the valuation of our deferred tax assets and liabilities; (4) increases in expenses not deductible for tax purposes, including transaction costs and impairments of goodwill in connection with acquisitions; (5) changes in the taxation of stock-based compensation; (6) changes in tax laws or the interpretation of such tax laws, and changes in generally accepted accounting principles; and (7) challenges to the transfer pricing policies related to our structure prior to the Domestication and Reorganization.

Changes in tax laws in the United States or foreign jurisdictions could materially increase our tax expense.

We are subject to income taxes in the United States and foreign jurisdictions. Changes to income tax laws and regulations, or the interpretation of such laws, in any of the jurisdictions in which we operate could significantly increase our effective tax rate and ultimately reduce our cash flows from operating activities and otherwise have a material adverse effect on our financial condition. Additionally, various levels of government are increasingly focused on tax reform and other legislative actions to increase tax revenue, and President Biden's campaign proposals included increasing the U.S. corporate income tax rate from 21% to 28%. Further changes in the tax laws of foreign jurisdictions could arise as a result of the base erosion and profit shifting project undertaken by the Organisation for Economic Co-operation and Development, which represents a coalition of member countries and recommended changes to numerous long-standing tax principles. If implemented by taxing authorities, such changes, as well as changes in U.S. federal and state tax laws or in taxing jurisdictions' administrative interpretations, decisions, policies, and positions, could have a material adverse effect on our business, results of operations, or financial condition.

General Risk Factors

Our business and operations would suffer in the event of system failures, security breaches or cyber-attacks.

Our computer systems, as well as those of various third parties on which we rely, or may rely on in the future, including our CRO's and other contractors, consultants, and law and accounting firms, may sustain damage from computer viruses, unauthorized access, data breaches, phishing attacks, cybercriminals, natural disasters, terrorism, war and telecommunication and electrical failures. We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. We have experienced phishing attacks in the past, which have not had a material impact on our operations, however, we may in the future experience material system failures or security breaches that could cause interruptions in our operations or result in a material disruption of our development programs. For example, the loss of nonclinical or clinical trial data from completed, ongoing or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability, suffer reputational damage, and the further development of our product candidates could be delayed.

If securities or industry analysts cease to publish research or reports about our business, or publish negative reports about our business, our stock price and trading volume could decline.

The trading market for our common stock depends, in part, on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. If our financial performance fails to meet analyst estimates or one or more of the analysts who cover us downgrade our common stock or change their opinion of our common stock, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline.

We have incurred and will continue to incur substantial costs as a result of operating as a public company, and our management has been and will be required to continue to devote substantial time to compliance with our public company responsibilities and corporate governance practices.

As a public company, we have incurred 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 listing requirements of Nasdaq and other applicable securities rules and regulations impose various requirements on public companies. Our management and other personnel devote a substantial amount of time to compliance with these requirements. Moreover, changing rules and regulations may increase our legal and financial compliance costs and make some activities more time-consuming and more costly. If, notwithstanding our efforts to comply with new or changing laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us, and our business may be harmed.

Further, failure to comply with these laws, regulations and standards may make it more difficult and more expensive for us to obtain directors' and officers' liability insurance, which could make it more difficult for us to attract and retain qualified members of our Board of Directors or members of senior management.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our principal and registered offices are located at 130 West 42nd St., 26th Floor, New York, New York 10036. In August 2020, we entered into a lease agreement for office space in New York, New York that commenced in December 2020 and expires in June 2026. In August 2019, we entered into a lease agreement for office space in Durham, North Carolina, which expires in November 2022.

We believe that all of our facilities are in good condition and are well maintained and that our current arrangements will be sufficient to meet our needs for the foreseeable future and that any required additional space will be available on commercially reasonable terms to meet space requirements if they arise.

Item 3. Legal Proceedings

From time to time, we may become involved in legal proceedings relating to claims arising from the ordinary course of business. We are not currently a party to any material legal proceedings, and we are not aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results or financial condition.

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 for Shares of Common Stock

Our shares of common stock began trading on the NYSE under the symbol "AXON" on June 11, 2015. Prior to that date, there was no public market for our shares of common stock. Effective September 6, 2017, we changed our listing to the Nasdaq Global Select Market and began trading under the symbol "AXON". Effective February 14, 2019, we changed our symbol to "AXGT" and effective November 13, 2020, we changed our symbol to "SIOX".

A 1-for-8 reverse stock split of our outstanding common stock was effected in May 2019 as approved by our Board of Directors and a majority of our shareholders. As such, all references to share and per share amounts in this Annual Report on Form 10-K have been retroactively restated to reflect the 1-for-8 reverse stock split, except for the authorized number of shares of our common stock and the par value per share, which were not affected. The reverse stock split reduced the number of the Company's shares of common stock issued and outstanding from approximately 182.2 million to 22.8 million as of March 31, 2019.

Stockholders

American Stock Transfer & Trust Company is the transfer agent and registrar for our shares of common stock. As of April 30, 2021, we had three holders of record of our shares of common stock. The actual number of shareholders is greater than this number of record holders and includes shareholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include shareholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid cash dividends on our shares of common stock. We anticipate that we will retain all of our future earnings, if any, for use in the expansion and operation of our business and do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our Board of Directors.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

Item 6. Selected Financial Data

In the table below, we provide you with our selected consolidated financial data for the periods presented. The information has been derived from our audited consolidated financial statements found elsewhere in this Annual Report on Form 10-K and in the other reports we have filed with the Securities and Exchange Commission ("SEC") under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). You should read the following selected consolidated financial data in conjunction with our consolidated financial statements and related notes included in this Annual Report on Form 10-K and "Item 7—Management's Discussion and Analysis of Financial Condition and Results of Operations" of this Annual Report on Form 10-K. The selected financial data in this section are not intended to replace our consolidated financial statements and the related notes. Our historical results are not necessarily indicative of our future results.

	Years Ended March 31,				
	2021	2020	2019	2018	2017
Statements of Operations Data:	(In thousands, except share and per share data)				
Operating expenses:					
Research and development expenses (includes $1,583, $2,772, $4,758, $16,597 and $19,186 of stock-based compensation expense for the years ended March 31, 2021, 2020, 2019, 2018 and 2017, respectively)	$ 24,903	$ 47,110	$ 87,552	$ 141,412	$ 134,778
General and administrative expenses (includes $2,909, $5,123, $11,671, $15,281 and $17,184 of stock-based compensation expense for the years ended March 31, 2021, 2020, 2019, 2018 and 2017, respectively)	17,294	22,061	39,466	71,906	45,721
Total operating expenses	42,197	69,171	127,018	213,318	180,499
Interest expense	799	4,377	7,530	7,545	1,143
Other (income) expense	(10,359)	(1,358)	(5,616)	(211)	369
Loss before income tax (benefit) expense	(32,637)	(72,190)	(128,932)	(220,652)	(182,011)
Income tax (benefit) expense	(212)	438	133	921	(1,060)
Net loss	$ (32,425)	$ (72,628)	$ (129,065)	$ (221,573)	$ (180,951)
Net loss per share of common stock — basic and diluted	$ (0.62)	$ (2.93)	$ (8.02)	$ (16.51)	$ (14.60)
Weighted average shares of common stock outstanding — basic and diluted	52,181,398	24,812,536	16,100,686	13,421,984	12,394,837

	As of March 31,				
	2021	2020	2019	2018	2017
Balance Sheet Data:	(In thousands)				
Cash and cash equivalents	$ 118,986	$ 80,752	$ 106,999	$ 154,337	$ 212,573
Working capital	121,485	53,387	71,085	111,687	173,422
Total assets	135,147	93,680	122,706	160,786	222,539
Long-term liabilities	932	79	22,994	42,925	51,436
Accumulated deficit	(791,069)	(758,644)	(686,016)	(556,951)	(335,143)
Total shareholders' equity	123,367	61,558	56,213	71,286	124,837

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the audited consolidated financial statements and the related notes thereto included elsewhere in this Annual Report on Form 10-K.

Overview

We are a clinical-stage company focused on developing gene therapies to radically transform the lives of patients with neurodegenerative diseases. We currently have three clinical-stage programs: (i) the AXO-AAV-GM1 program for the treatment of GM1 gangliosidosis in which five patients have been dosed in the late-infantile/juvenile (Type II) low-dose cohort of stage 1, and we have dosed two late-infantile/juvenile (Type II) patients in the higher dose cohort of the study and expect to continue to dose Type II patients and initiate the low-dose infantile (Type I) patients in calendar year 2021; (ii) the AXO-AAV-GM2 program for the treatment of GM2 gangliosidosis (including Tay-Sachs and Sandhoff diseases) for which we received clearance for the IND from the FDA in November 2020, and in which we dosed the first infantile patient in January 2021; and (iii) the AXO-Lenti-PD program for the treatment of Parkinson's disease, comprised of the ProSavin Phase 1/2 study in which 15 patients were previously dosed and the AXO-Lenti-PD SUNRISE-PD study in which we have dosed two patients in Cohort 1 of the dose-escalation study and four patients in Cohort 2.

We are dedicated to realizing the potential of gene therapies to offer transformative patient outcomes in areas of high unmet medical need and extending the reach of gene therapies to highly prevalent neurodegenerative disorders like Parkinson's disease. We have assembled a portfolio of gene therapies in partnership with leading scientific institutions and have built a team with extensive experience in the gene therapy space. Our team pursues new innovations in vector design and delivery to optimize our investigational gene therapy products for safety, potency, durability, and immunologic response. We will continue to build integrated internal development capabilities from product development through commercialization and focus on accelerating the pace of product development in the clinic. As part of our ongoing business strategy, we continue to explore potential opportunities to acquire or license new product candidates as well as opportunities for partnership or collaboration on our existing products in development. Our vision is to build the world's leading gene therapy company for the treatment of neurodegenerative diseases by progressing our current programs and identifying, developing and commercializing other novel gene therapy treatments for neurodegenerative diseases.

See section "Our Key Agreements" within "Item 1—Business" of this Annual Report on Form 10-K for information regarding our license agreement with the University of Massachusetts Medical School (the "UMMS Agreement" and "UMMS", respectively) and our license agreement with Oxford Biomedica (UK) Ltd. (the "Oxford Agreement" and "Oxford", respectively).

The Domestication

We have substantially completed our previously disclosed corporate transformation to align corporate structure and governance with current and future business activity, including significantly reducing the number of our subsidiaries. On November 12, 2020, Axovant Gene Therapies Ltd. ("AGT") discontinued as a Bermuda exempted company pursuant to Section 132G of the Companies Act 1981 of Bermuda, and pursuant to Section 388 of the General Corporation Law of the State of Delaware (the "DGCL"), continued its existence under the DGCL as a corporation named Sio Gene Therapies Inc. ("Sio") organized in the State of Delaware (the "Domestication"). The Domestication effected a change in our jurisdiction of incorporation, and other changes of a legal nature, including changes in our organizational documents. Our consolidated business, operations, assets and liabilities did not change upon effectiveness of the Domestication. However, following the Domestication, the principal executive offices and registered offices of Sio are located at 130 West 42nd St, 26th Floor, New York, New York 10036, and the telephone number for Sio at its principal executive offices is 1-877-746-4891. The fiscal year end of Sio Gene Therapies Inc. following the Domestication remains at March 31. In addition, our directors and executive officers immediately after the Domestication were the same individuals who were directors and executive officers, respectively, immediately prior to the Domestication.

In the Domestication, each of our currently issued and outstanding common shares automatically converted by operation of law, on a one-for-one basis, into shares of Sio common stock. Consequently, upon the effectiveness of the Domestication, each holder of an AGT common share instead holds a share of Sio common stock representing the same proportional equity interest in Sio as that shareholder held in AGT and representing the same class of shares. The number of shares of Sio common stock outstanding immediately after the Domestication is the same as the number of common shares of AGT. outstanding immediately prior to the Domestication. In connection with the Domestication, we adopted a new certificate of incorporation, bylaws and form of common stock certificate, copies of which were filed as Exhibits 3.1, 3.2 and 4.1, respectively, to our Report on Form 8-K12G3 filed with the SEC on November 13, 2020.

COVID-19 Business Update

We are continuing to closely monitor the impact of the global COVID-19 pandemic on our business and are taking proactive efforts to minimize the risks to the health and safety of our patients, study investigators and employees, as well as to maintain business continuity. We believe that the measures we are implementing are appropriate, reflecting both regulatory and public health guidance, to maintain business continuity. We will continue to closely monitor and seek to comply with guidance from governmental authorities and adjust our activities as appropriate.

In the conduct of our business activities, we are also taking actions designed to protect the safety and well-being of patients, healthcare workers and employees. For patients already enrolled in our clinical trials, we are working closely with clinical trial investigators and site staff to continue treatment in compliance with trial protocols and to uphold trial integrity, while working to observe government and institutional guidelines designed to safeguard the health and safety of patients, clinical trial investigators and site staff. We are continuing to evaluate clinical trial site initiations and patient enrollment on a case-by-case and patient-by-patient basis in coordination with clinical trial investigators and site staff. Some clinical trial sites, both within the United States and the United Kingdom, continue to screen patients in our clinical trials, and new patients are being enrolled when appropriate. Our clinical trial progression, dosing, patient enrollment and related activities may be delayed, and reporting of some clinical data may be incomplete or delayed if patients enrolled in our clinical trials are unable to fully participate in all necessary measurement protocols, due to concerns among patients about participating in clinical trials during a pandemic, or remaining restrictions imposed by institutions or local, state or national governments, among other factors. Some patients may have difficulty following certain aspects of clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. For example, patients in our clinical trials for AXO-AAV-GM1 and AXO-AAV-GM2 are infants, often with advanced disease, who may not be able to safely participate in clinical trials for these product candidates during the COVID-19 pandemic or if they have not received or are not eligible to receive COVID-19 vaccinations. Additionally, our clinical trial for AXO-Lenti-PD can involve elderly patients with advanced disease who may be unable to participate in clinical assessments at our research sites in the United Kingdom. For example, because of the COVID-19 pandemic and a patient refusal, two out of four patients in the second cohort of our Phase 2 clinical trial of AXO-Lenti-PD at our United Kingdom clinical trial sites were unable to participate in Unified Parkinson’s Disease Rating Scale ("UPDRS") assessments and the mandatory washout of background levodopa therapy at the six-month time point. However, all four of these subjects were able to complete all other efficacy assessments at the six-month timepoint, including the patient-recorded Hauser diaries. We are working with sites and investigators to ensure safe and ethical data collection at future time points through the pandemic in accordance with regulatory guidance. While the COVID-19 pandemic has not resulted in a significant delay to our clinical development timelines to-date, the global pandemic of COVID-19 continues to evolve, and could materially impact our clinical development and any future commercialization timelines.

Our business, including patient enrollment and CMC manufacturing efforts for our clinical trials, could continue to be adversely impacted by health epidemics wherever we have clinical trial sites or other business operations. In addition, health epidemics could cause significant disruption in the operations of third-party manufacturers, CROs and other third parties upon whom we rely. We are also dependent on an international supply chain for products to be used in our clinical trials and, if approved by the regulatory authorities, for commercialization. While the COVID-19 pandemic has not significantly adversely impacted our business operations, international supply chain, productivity or clinical development timelines to-date, the reintroduction of health directives and recommendations to reduce the spread of the disease, including shelter-in-place directives and executive orders directing that all non-essential businesses close their physical operations may continue to negatively impact productivity, disrupt our business or international supply chain and delay our clinical programs and timelines in the future, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course.

The ultimate impact and evolving effects of the COVID-19 pandemic or a similar health epidemic are highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could harm our operations, and we will continue to monitor the COVID-19 situation closely. For additional information about risks and uncertainties related to the COVID-19 pandemic that may impact our business, financial condition and results of operations, see the section titled “Risk Factors” under Part I, Item 1A in this Annual Report on Form 10-K.

Financial Operations Overview

Revenue

We have not generated any revenue from the sale of any products, and we do not expect to generate any revenue unless and until we obtain regulatory approval of and begin to commercialize one of our gene therapy product candidates in development.

Research and Development Expense

Since our inception, our operations have primarily been focused on organizing and staffing our company, raising capital, and acquiring, preparing for and advancing our product candidates into clinical development. Our research and development expenses include program-specific costs, as well as unallocated internal costs.

Program-specific costs include:

- direct third-party costs, which include expenses incurred under agreements with CROs and contract manufacturing organizations, the cost of consultants who assist with the development of our product candidates on a program-specific basis, investigator grants, sponsored research, manufacturing costs in connection with producing materials for use in conducting nonclinical and clinical studies, and any other third-party expenses directly attributable to the development of our product candidates; and

- upfront payments for the purchase of in-process research and development and milestone payments, which include costs incurred under our agreements with UMMS and Oxford, as well as costs incurred for our discontinued AXO-AAV-OPMD program.

Unallocated internal costs include:

- stock-based compensation expense for research and development personnel;

- personnel-related expenses, which include employee-related expenses, such as salaries, benefits and travel expenses, for research and development personnel; and

- other expenses, which includes the cost of consultants who assist with our research and development but are not allocated to a specific program.

Research and development activities will continue to be central to our business model and will vary significantly based upon the success of our programs and the achievement of milestones requiring payments to our partners, UMMS and Oxford. We plan to substantially increase our research and development expenses in the fiscal year ending March 31, 2022, as we continue the enrollment of patients in our GM1 and GM2 clinical trials, and commission the manufacturing of clinical supplies for these trials. As well, it is possible that Oxford will complete the development of a suspension-based manufacturing process for AXO-Lenti-PD this fiscal year, and, as a result, we will be responsible for one or more batches of clinical supplies for this program.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

The duration, costs and timing of clinical trials of our products in development and any other product candidates will depend on a variety of factors that include, but are not limited to, the following:

- the number of trials required for approval;

- the per patient trial costs;

- the number of patients who participate in the trials;

- the number of sites included in the trials;

- the countries in which the trials are conducted;

- the length of time required to enroll eligible patients;

- the dose that patients receive;

- the drop-out or discontinuation rates of patients;

- the potential additional safety monitoring or other studies requested by regulatory agencies;

- the duration of patient follow-up;
- any delays in key trial activities and patient enrollment or diversion of healthcare resources as a result of the COVID-19 pandemic;
- production shortages or other supply interruptions in clinical trial materials resulting from the COVID-19 pandemic;
- the timing and receipt of regulatory approvals; and
- the efficacy and safety profile of the product candidates.

In addition, the probability of success of our gene therapy products in development and any other product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability. We may never succeed in achieving regulatory approval of our gene therapy product candidates for any indication in any country. As a result of the uncertainties discussed above, we are unable to determine in advance the duration and completion costs of any clinical trial we conduct, or when and to what extent we will generate revenue from the commercialization and sale of our products in development or other product candidates, if at all.

General and Administrative Expense

General and administrative expenses consist primarily of stock-based compensation, including expense allocated to us related to common share awards and options issued by RSL to certain of our employees and to certain employees of RSL and certain of its subsidiaries; legal and accounting fees; consulting services; and employee-related expenses such as salaries, benefits and travel expenses, for general and administrative personnel. In prior periods, a significant component of our total stock-based compensation expense related to allocated costs from RSL for common share awards and options issued by RSL to certain of our employees, as well as to certain employees of RSL and certain of its subsidiaries. Stock-based compensation expense is allocated to us from RSL based upon the relative percentage of time utilized by certain employees of RSL and certain of its subsidiaries on our matters, as well as based upon our employees that hold such RSL common share awards and options. These common share awards and options are fair valued on the date of grant with expense recognized over the requisite service period. The fair value of each such option is estimated on the date of grant using the Black-Scholes closed-form option-pricing model. These common share awards and options are subject to specified vesting schedules and requirements (a mix of time-based, performance-based and corporate event-based, including targets for RSL's post-initial public offering market capitalization and future financing events), which could result in significant stock-based compensation expense allocated to us from RSL in the future, if achieved.

We anticipate that our general and administrative expenses will at least approximate those incurred during the fiscal year ended March 31, 2021 in the near term.

Results of Operations for the Years Ended March 31, 2021 and March 31, 2020

The following table summarizes our results of operations for the years ended March 31, 2021 and March 31, 2020 (in thousands):

	Years Ended March 31,	
	2021	2020
Operating expenses:		
Research and development expenses (includes $1,583 and $2,772 of stock-based compensation expense for the years ended March 31, 2021 and 2020, respectively)	$ 24,903	$ 47,110
General and administrative expenses (includes $2,909 and $5,123 of stock-based compensation expense for the years ended March 31, 2021 and 2020, respectively)	17,294	22,061
Total operating expenses	42,197	69,171
Interest expense	799	4,377
Other income	(10,359)	(1,358)
Income tax (benefit) expense	(212)	438
Net loss	$ (32,425)	$ (72,628)

Research and Development Expenses

For the years ended March 31, 2021 and 2020, our research and development expenses consisted of the following (in thousands):

	Years Ended March 31,		
	2021	2020	Change
Program-specific costs:			
AXO-Lenti-PD	$ 5,668	$ 22,182	$ (16,514)
AXO-AAV-GM1 and AXO-AAV-GM2	6,907	9,785	(2,878)
AXO-AAV-OPMD (discontinued)	—	1,791	(1,791)
Unallocated internal costs:			
Stock-based compensation	1,583	2,772	(1,189)
Personnel-related	7,058	7,149	(91)
Other	3,687	3,431	256
Total research and development expenses	$ 24,903	$ 47,110	$ (22,207)

Research and development expenses were $24.9 million for the year ended March 31, 2021 compared to $47.1 million for the year ended March 31, 2020. The $22.2 million decrease was primarily related to $14.0 million in certain nonrecurring development and regulatory milestones achieved in the prior year for the AXO-Lenti-PD ($13.0 million) and AXO-AAV-GM2 programs. In addition, there were reduced program-specific research and development costs of $7.2 million due to (i) lower AXO-Lenti-PD clinical expenses as the enrollment of Cohort 2 was completed in the prior year, as well as lower manufacturing expenses due to the delays at Oxford, (ii) reduced clinical and manufacturing expenses while awaiting FDA clearance of the IND for the AXO-AAV-GM2 program, and (iii) the discontinuation of the AXO-AAV-OPMD program during the prior year.

General and Administrative Expenses

General and administrative expenses were $17.3 million for the year ended March 31, 2021 and $22.1 million for the year ended March 31, 2020. The decrease of $4.8 million was primarily related to reductions in stock-based compensation expense of $2.2 million primarily attributable to lower grant date fair values per share for equity awards and lower headcount and personnel costs (including severance) of $1.3 million attributable to lower headcount.

Interest Expense

Interest expense was $0.8 million and $4.4 million for the years ended March 31, 2021 and 2020, respectively. The decrease in interest expense during the current year was primarily due to the April 2020 prepayment of the $15.7 million outstanding principal balance on our loan and security agreement with Hercules Capital, Inc. ("Hercules").

Other Income

Other income was $10.4 million and $1.4 million for the years ended March 31, 2021 and 2020, respectively. Other income for the year ended March 31, 2021 included income of approximately $11.3 million associated with gains on our investment in Arvelle Therapeutics B.V. ("Arvelle") that was sold in February 2021, which was partially offset by foreign exchange losses. Other income for the year ended March 31, 2020 consisted primarily of foreign exchange gains and interest income.

Liquidity and Capital Resources

Sources of Liquidity

Since our initial public offering in June 2015, our operations have been financed primarily through sales of common stock and pre-funded warrants, as well as borrowings under our credit facilities. As of March 31, 2021, we had $119.0 million of cash and cash equivalents available to us, and in April 2020, we prepaid the remaining outstanding principal balance, equal to $15.7 million, together with $0.3 million of accrued interest, fees and other amounts due under our loan and security agreement with Hercules.

Capital Requirements

We are currently in the clinical stage of operations and have not yet achieved profitability. We expect to continue to incur significant operating and net losses, as well as negative cash flows from operations, for the foreseeable future as we continue to develop our gene therapy product candidates and prepare for potential future regulatory approvals and commercialization of our products. We have not generated any revenue to date and do not expect to generate product revenue unless and until we successfully complete development and obtain regulatory approval for at least one of our gene therapy product candidates. Our current cash and cash equivalents balance will also not be sufficient to complete all necessary development activities and commercially launch our products.

We expect to spend substantial amounts to complete the development of, seek regulatory approvals for and commercialize our product candidates. In addition, as part of our business development strategy, we generally structure our license agreements and collaboration agreements so that a significant portion of the total license cost is contingent upon the successful achievement of specified development, regulatory or commercial milestones. As a result, we will require cash to make payments upon achievement of these milestones under these agreements. Based on our anticipated timeline for the achievement of development, regulatory and commercial milestones, we do not expect significant milestone payments under our license and collaboration agreements to come due prior to March 31, 2022.

Because the length of time and activities associated with successful development of our product candidates are highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. However, we anticipate that our current cash and cash equivalents balance is sufficient to fund our clinical milestones beyond the expected dates of major upcoming milestones for our AXO-AAV-GM1 gene therapy program for the treatment of GM1 gangliosidosis. 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 trials of our product candidates;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, the EMA, or the PMDA, and other comparable foreign regulatory authorities;
- the achievement of certain development, regulatory and commercialization milestones that give rise to milestone and royalty payments to licensors;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of obtaining necessary intellectual property and defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates or any future product candidates;
- the effect of competing technological and market developments;
- the cost and timing of completion of clinical-stage and commercial-scale manufacturing activities, including costs that may result from delays in the development of a suspension-based manufacturing process by our partner, Oxford;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates in regions where we choose to commercialize our products on our own; and
- the initiation, progress, timing and results of our commercialization of our product candidates, if approved for commercial sale.

For the years ended March 31, 2021 and March 31, 2020, we incurred net losses of $32.4 million and $72.6 million, respectively. As of March 31, 2021, our cash and cash equivalents totaled $119.0 million and our accumulated deficit was $791.1 million. We estimate that our current cash and cash equivalents balance is sufficient to support operations beyond the twelve-month period following the date that the accompanying consolidated financial statements were issued, including beyond the expected dates of major upcoming milestones for our AXO-AAV-GM1 gene therapy program for the treatment of GM1 gangliosidosis. As such, we have determined that there is no longer substantial doubt about our ability to continue as a going concern for the one-year period following the date that the accompanying consolidated financial statements were issued. These estimates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

Until such time, if ever, as we can generate substantial revenue from sales of our products in development, we expect to finance our cash needs through a combination of equity offerings, debt financings and potential collaboration, license or development agreements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. In addition, 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, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

In order to meet our long-term operating requirements, we will need, among other things, additional capital resources. We continually assess multiple options to obtain additional funding to support our operations, including proceeds from offerings of our equity securities or debt, or transactions involving product development, technology licensing or collaboration arrangements, or other sources of capital to complete our currently planned development programs. Sources of a sufficient amount of financing may not be available to us on favorable terms, if at all, and our ability to raise additional capital may be adversely impacted by potentially worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. In addition, extreme price and volume fluctuations in the stock market in general, and the Nasdaq Global Select Market, in particular, have resulted in volatile and sometimes decreased stock prices for many companies, including us. Broad market and industry factors, including worsening economic conditions and other adverse effects or developments relating to the evolving effects of the COVID-19 pandemic, may negatively affect the market price of our common stock, regardless of our actual operating performance, and impact our ability to raise sufficient additional capital on acceptable terms, if at all. If we are unable to raise additional funds 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.

At-the-Market Equity Offering Program

We have engaged SVB Leerink LLC as our agent to sell shares of our common stock from time to time through an at-the-market equity offering program. SVB Leerink LLC is entitled to compensation for its services in an amount equal to 3% of the gross proceeds of any of our shares of common stock sold. As of March 31, 2021, we have sold approximately 29.7 million shares of common stock for total proceeds of approximately $90.5 million, net of brokerage fees, under the sales agreement since April 2020. Subsequent to March 31, 2021, we have sold approximately 0.2 million shares of common stock for total proceeds of approximately $0.5 million under the sales agreement, net of brokerage fees.

Cash Flows

The following table sets forth a summary of our cash flows for each of the periods shown (in thousands):

	Years Ended March 31,	
	2021	2020
Net cash used in operating activities	$ (46,589)	$ (67,473)
Net cash provided by (used in) investing activities	12,386	(255)
Net cash provided by financing activities	73,621	41,481

Operating Activities

Cash flows from operating activities consist of net loss adjusted for non-cash items, including depreciation and stock-based compensation expenses, as well as the effect of changes in working capital and other activities.

For the year ended March 31, 2021, net cash used in operating activities was $46.6 million and was primarily attributable to a net loss of $32.4 million, which includes costs incurred for research and development activities, including CRO fees, manufacturing, regulatory and other clinical trial costs, as well as our general and administrative expenses, in addition to other income of $11.3 million associated with gains on our investment in Arvelle, an increase of $4.4 million in prepaid expenses and other current assets and decreases of $3.1 million in accounts payable and $2.1 million in accrued expenses, which were partially offset by $4.5 million of non-cash stock-based compensation expense and $1.5 million of operating lease right-of-use asset amortization expense

For the year ended March 31, 2020, net cash used in operating activities was $67.5 million and was primarily attributable to a net loss of $72.6 million, which includes costs incurred for research and development activities, including $14.0 million for development and regulatory milestones achieved, CRO fees, manufacturing, regulatory and other clinical trial costs, as well as our general and administrative expenses, in addition to a decrease of $9.3 million in accrued expenses, which were partially offset by $7.9 million of non-cash stock-based compensation expense, a decrease of.$2.9 million in prepaid expenses and other current assets and an increase of $2.7 million in accounts payable.

Investing Activities

For the year ended March 31, 2021, net cash provided by investing activities was $12.4 million, consisting of proceeds of $12.8 million from the sale of our long-term investment in Arvelle that was partially offset by purchases of fixed assets.

For the year ended March 31, 2020, net cash used in investing activities was $0.3 million, consisting of purchases of fixed assets.

Financing Activities

For the year ended March 31, 2021, net cash provided by financing activities was $73.6 million and consisted primarily of $89.2 million of net proceeds from the issuance and sale of our shares of common stock under our share sales agreement with SVB Leerink LLC, partially offset by $15.7 million of principal payments made on long-term debt.

For the year ended March 31, 2020, net cash provided by financing activities was $41.5 million and consisted primarily of $70.8 million of net proceeds from the issuance and sale of our shares of common stock and pre-funded warrants in a public offering, partially offset by $29.6 million of payments made on long-term debt.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under the SEC's rules.

Contractual Obligations

The following table provides information with respect to our outstanding contractual obligations as of March 31, 2021:

Contractual Obligations (in thousands) [1]	Total	Under 1 year	1-3 years	3-5 years	Over 5 years
Real property lease obligations [2]	$ 1,561	$ 327	$ 567	$ 667	$ —
Total	$ 1,561	$ 327	$ 567	$ 667	$ —

[1] This table does not include any milestone and royalty payments which may become payable to third parties for which the timing and likelihood of such payments are not known. Potential milestone and royalty payments are described below under "-Milestone and Royalty Payments."

[2] Amounts due, net of prepayments. Real property lease obligations are described below under "-Real Property Leases."

In addition, we have entered into services agreements with third parties for pharmaceutical manufacturing and research activities in the normal course of business, which can generally be terminated by us with 30- or 60-days' written notice, unless otherwise indicated. These cancellable contracts are not included in the table above. Further, certain of our manufacturing agreements could require early termination and wind-down payments due from us upon either the termination of our clinical trials or if we unilaterally terminate such agreements for convenience, which agreements are not included in the table above.

Milestone and Royalty Payments to UMMS and Oxford

In addition to the amounts shown in the above table, we are contractually obligated to make payments to UMMS totaling up to $24.5 million upon the achievement of specified development and regulatory milestones, including development and regulatory milestones of $1.0 million and $1.0 million that were achieved in February 2019 and October 2019, respectively, and that were paid during the fiscal year ended March 31, 2020, and up to $39.8 million upon the achievement of specified commercial milestones for AXO-AAV-GM1 and AXO-AAV-GM2. We are also obligated to pay UMMS tiered mid-single digit royalties based on yearly net sales of the licensed products, subject to a specified annual minimum amount. Additionally, we will pay UMMS a percent of any revenues we receive from any third-party sublicenses to licensed products at rates ranging in the mid-single digits to mid-teens. We could also be obligated to make payments to Oxford totaling up to $55.0 million upon the achievement of specified development milestones, including certain development milestones that were achieved in April 2019 that resulted in a $13.0 million net payment due to Oxford that was paid during the year ended March 31, 2020, and up to $757.5 million upon the achievement of specified regulatory and sales milestones, as well as a tiered royalty from 7% to 10% of the yearly aggregate net sales of the underlying gene therapy products.

These payments are contingent upon the occurrence of certain future events and, given the nature of those events, it is unclear when, if ever, we may be required to make sure payments, and with respect to royalty payments, what the total amount of such payments will be. Further, the timing of any of the foregoing future payments is not reasonably estimable. For those reasons, these contingent payments have not been included in the table above.

Real Property Leases

In June 2017, we entered into a license agreement with a third-party to lease office space in New York, New York that expired in January 2021, and we also leased office space in Princeton, New Jersey under an agreement that expired in October 2020. In October 2019, we entered into an agreement with a third-party to lease office space in Durham, North Carolina under a lease agreement expiring in November 2022, and in August 2020, we entered into a lease agreement with a third-party for an office facility in New York, New York that commenced in December 2020 and expires in June 2026. For the years ended March 31, 2021 and March 31, 2020, we incurred $1.6 million and $1.8 million, respectively, in rent expense under these agreements.

Recent Accounting Pronouncements

For detailed information regarding recently issued accounting pronouncements and the expected impact on our financial statements, refer to Note 2 "Summary of Significant Accounting Policies," in the accompanying notes to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Critical Accounting Policies and Significant Judgments and Estimates

Our 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 U.S. generally accepted accounting principles ("GAAP"). The preparation of these consolidated financial statements and accompanying notes requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities as of the dates of the balance sheets and the reported amounts of expenses during the reporting periods. In accordance with U.S. GAAP, we evaluate our estimates and judgments on an ongoing basis. Significant estimates include research and development accruals. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We define our critical accounting policies as those under U.S. GAAP that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles.

Our significant accounting policies are more fully described in Note 2, "Summary of Significant Accounting Policies," to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. Not all of these significant accounting policies, however, require that we make estimates and assumptions that we believe are "critical accounting estimates." We believe that our estimates relating to research and development accruals have the greatest potential impact on our consolidated financial statements and consider these to be our critical accounting policies and estimates and are "critical accounting estimates."

Research and Development Accruals

Research and development costs are expensed as incurred. Clinical study costs are accrued over the service periods specified in the contracts and adjusted as necessary based upon an ongoing review of the level of effort and costs actually incurred. The Company’s assessment of the completeness of the information is subject to variability and uncertainty. In addition, in certain circumstances, the determination of the nature and amount of services that have been received during the reporting period requires judgment as the timing and pattern of vendor invoicing does not correspond to the level of services provided. Payments for a product license prior to regulatory approval of the product and payments for milestones achieved prior to regulatory approval of the product are expensed in the period incurred as research and development. Milestone payments made in connection with final regulatory approvals are capitalized and amortized to cost of revenue over the remaining useful life of the asset. Research and development costs are charged to expense when incurred and currently primarily consist of the development and regulatory milestones achieved for our AXO-AAV-GM1, AXO-AAV-GM2 and AXO-Lenti-PD gene therapy programs, as well as research and development materials acquired from UMMS and Oxford and expenses from third parties who conduct research and development activities on our behalf. We expense in-process research and development projects acquired as asset acquisitions which have not reached technological feasibility, and which have no alternative future use.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Market risk is the potential loss arising from adverse changes in market rates and market prices such as interest rates, foreign currency exchange rates, and changes in the market value of equity instruments. As of March 31, 2021, we had cash and cash equivalents of $119.0 million, with cash consisting of non-interest-bearing deposits denominated in the U.S. dollar, Swiss franc and Euro, and cash equivalents consisting of interest-bearing money market fund deposits denominated in the U.S. dollar, which are invested in debt securities issued or guaranteed by the U.S. government and repurchase agreements fully collateralized by U.S. Treasury and U.S. government securities. We have policies requiring us to invest in high-quality issuers, limit our exposure to any individual issuer, and ensure adequate liquidity. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash equivalent investments are in the form of money market funds and marketable securities and are invested in U.S. Treasury obligations. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

Item 8. Financial Statements and Supplementary Data

All financial statements and schedules required to be filed hereunder are listed in the Index to Financial Statements and set forth in Item 15 of this Annual Report on Form 10-K and are incorporated herein by reference.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Under the supervision of our principal executive officer and principal financial officer, we evaluated the effectiveness of our disclosure controls and procedures as of March 31, 2021, the end of the period covered by this report. The term "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")), means controls and other procedures of a company that are designed to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Disclosure controls and procedures include, without limitation, controls and procedures designed to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow for timely decisions regarding required disclosure. Based on this evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of March 31, 2021 at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act). Our management conducted an evaluation of the effectiveness of our internal control over financial reporting as of March 31, 2021, based on the criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Based on the results of our evaluation, management concluded that our internal control over financial reporting was effective as of March 31, 2021.

Inherent Limitations on Effectiveness of Controls

Our management, including our principal executive officer and principal financial officer, does not expect that our disclosure controls and procedures or our internal controls will prevent all error and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within Sio Gene Therapies Inc. have been detected.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm pursuant to the rules of the SEC that permit us to provide only management's report on internal control over financial reporting in this report, as we were a smaller reporting company as defined in the rules and regulations of the SEC as of March 31, 2021.

Changes in Internal Control over Financial Reporting

No changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal quarter ended March 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III.

Item 10. Directors, Executive Officers and Corporate Governance

Directors

Our Board of Directors (the "Board") presently has seven members. Each director is elected to serve a one-year term, with all directors subject to annual election. Vacancies on the Board may be filled by the Board or by the shareholders in a general meeting. A director elected to fill a vacancy, including vacancies created by an increase in the number of directors, will serve for the remainder of the full term.

Berndt Modig, Senthil Sundaram, Pavan Cheruvu, M.D., Atul Pande, M.D., Frank Torti, M.D. and Eric Venker, M.D, Pharm.D. are each current directors who were previously elected by our shareholders. Kristiina Vuori, M.D., Ph.D. was appointed to the Board in October 2020 to fill an existing vacancy. Ilan Oren was not nominated to stand for re-election at our annual meeting of shareholders for 2020. Effective September 24, 2020, the date of such meeting, Mr. Oren is no longer a member of our Board.

The following table identifies our directors, as well as the position they hold, any committee membership, and their ages as of April 30, 2021:

Name	Age	Director Since	Position	Audit Committee	Compensation Committee	Nominating and Corporate Governance Committee
Frank Torti, M.D.	42	2018	Chairperson			
Atul Pande, M.D.	66	2015	Lead Independent Director	✓	✓	✓*
Pavan Cheruvu, M.D.	39	2018	Chief Executive Officer and Director			
Berndt Modig	62	2015	Director	✓	✓*	
Senthil Sundaram	42	2019	Director	✓*		✓
Eric Venker, M.D., Pharm.D.	34	2020	Director			
Kristiina Vuori, M.D., Ph.D.	53	2020	Director			✓

* Chairperson.

Below is a brief biography of each director.

Frank Torti, M.D.

Dr. Torti has served as Chairperson of the Board since September 2018. Dr. Torti has served as the Vant Chair of Roivant Sciences, Inc., or RSI, which is a wholly owned subsidiary of our affiliate, RSL, since January 2020. In this capacity he is responsible for the biopharmaceutical companies in the Roivant family and serves as Chairperson of the boards of directors of those companies. He previously served as Vant Investment Chair of RSI, from August 2018 to December 2019. Prior to joining RSI, from August 2007 to August 2018, Dr. Torti served as a Partner of New Enterprise Associates, or NEA, specializing in investments in healthcare. Prior to joining NEA, Dr. Torti worked for the Duke University Center for Clinical & Genetic Economics from 2002 to 2005 in various capacities, where he was involved in clinical trials research and economic evaluations of multinational clinical trials. Dr. Torti presently serves as Chairperson of the boards of directors of Arbutus Biopharma Corp., Immunovant Inc., and several private biopharmaceutical companies. He has previously served on the boards of directors of numerous development and commercial stage public and private healthcare companies, including Annexon Biosciences, Inc., Eargo Inc., Galera Therapeutics, Inc., Myovant Sciences Ltd., NeoTract, Inc., Urovant Sciences Ltd, and others. Dr. Torti earned an M.D. from the University of North Carolina School of Medicine, an M.B.A. from Harvard Business School and a B.A. from the University of North Carolina. Our Board of Directors believes that Dr. Torti’s extensive experience in healthcare investing, as well as his operational experience and clinical trial background, qualifies him to serve on the Board.

Atul Pande, M.D.

Dr. Pande has served as a member of the Board since March 2015 and currently serves as our Lead Independent Director. Dr. Pande has served as Chief Medical Advisor of PureTech Health plc since February 2018, and previously served as its Chief Medical Officer since February 2017 and a Senior Advisor from July 2016 through February 2017. Dr. Pande has also served as President and Chief Executive Officer of Verity BioConsulting LLC, a drug development consulting firm, since 2014. He previously served as Chief Medical Officer of Tal Medical, Inc., a clinical-stage medical device company, from December 2014 to December 2017. From 2007 to April 2014, Dr. Pande was Senior Vice President and Senior Advisor, Pharmaceutical R&D at GlaxoSmithKline plc, a pharmaceutical company. He has also held senior roles at Pfizer Inc., a multinational pharmaceutical company, Parke-Davis/Warner-Lambert, a subsidiary of Pfizer Inc. and Lilly Research Laboratories, a global pharmaceutical research organization and division of Eli Lilly & Co., where he was involved in the development of numerous central nervous system drugs. Dr. Pande is currently a director of Autifony Therapeutics Limited, a biotechnology company, Karuna Therapeutics, Inc., a biopharmaceutical company, Perception Neurosciences, a biopharmaceutical company, and Immunovant Inc., a biopharmaceutical company, and he previously served as a director of Heptares Therapeutics Ltd., a biotechnology company now a part of the Sosei Group. He also serves on the Scientific Advisory Boards of Cennerv Pharma PTE LTD and Centrexion Corporation. Dr. Pande is a fellow of several professional societies, including the American Psychiatric Association. He has published over 50 peer-reviewed scientific papers and numerous abstracts, book chapters and book reviews. Dr. Pande received his MBBS (Bachelor of Medicine, Bachelor of Surgery) and his M.D. from the University of Lucknow, India and completed his research fellowship training in psychiatry at the University of Michigan Medical School and his postgraduate specialty training and psychiatry residency program at Western University. We believe that Dr. Pande's medical background and significant knowledge of the life sciences industry qualify him to serve on the Board.

Pavan Cheruvu, M.D.

Dr. Cheruvu has served as our Chief Executive Officer since November 2020 and as a member of the Board since September 2018, and served as the Principal Executive Officer of Axovant Gene Therapies Ltd. from February 2018 until November 2020 and as the Chief Executive Officer of Axovant Sciences, Inc. from February 2018 until December 2020. Prior to joining us, Dr. Cheruvu worked at RSI since October 2015, and was appointed to RSI's executive leadership team in September 2017. Dr. Cheruvu completed his residency in internal medicine at Johns Hopkins Hospital and continued his training in a clinical fellowship in cardiovascular medicine at the University of California, San Francisco. Prior to his medical training, Dr. Cheruvu worked as a management consultant at McKinsey & Company from June 2008 through June 2011, where he focused on biopharmaceutical strategy. Dr. Cheruvu received his B.S.E. in Biomedical Engineering, B.S.E. in Electrical Engineering, and A.B. in Chemistry from Duke University, his M.Sc. in Computer Science from Oxford University and his M.D. from Harvard Medical School. We believe that Dr. Cheruvu's experience as a life sciences investor and experience in the biopharmaceutical industry qualify him to serve on the Board.

Berndt Modig

Mr. Modig has served as a member of the Board since March 2015. Since March 2016, Mr. Modig has served as Chief Executive Officer of Pharvaris N.V., a public clinical stage biotechnology company focusing on rare diseases. He served as Chief Financial Officer of Prosensa Holding N.V., a pharmaceutical company, from March 2010 until its acquisition by BioMarin Pharmaceutical Inc. in January 2015. From October 2003 to November 2008, Mr. Modig was Chief Financial Officer at Jerini AG, a pharmaceutical company, where he directed private financing rounds, its initial public offering in 2005, and its acquisition by Shire plc, a biopharmaceutical company acquired by Takeda Pharmaceutical Company, in 2008. Before that, Mr. Modig served as Chief Financial Officer at Surplex AG, a reseller of used industrial equipment, from 2001 to 2003, and as Finance Director Europe of U.S.-based Hayward Industrial Products Inc., a thermoplastic valve manufacturer, from 1999 to 2001. In previous positions, Mr. Modig was a partner in the Brussels-based private equity firm Agra Industria from 1994 to 1999 and a Senior Manager in the Financial Services Industry Group of Price Waterhouse LLP in New York from 1991 to 1994. Mr. Modig currently serves as a director of Pharvaris N.V., a public clinical stage biotechnology company. He also serves as chair of the audit committee and as a director of Centogene N.V., a public biopharmaceutical company. He also previously served on (i) the board of directors of Kiadis Pharma N.V., a public biopharmaceutical company, from June 2016 to April 2021, (ii) the board of directors of Auris Medical Holding Ltd., a pharmaceutical company, from April 2014 to March 2018, and (iii) the board of directors of Affimed N.V., a public biopharmaceutical company, from September 2014 to August 2020. Mr. Modig received his bachelor's degree in business administration, economics and German from the University of Lund, Sweden and his M.B.A. from INSEAD, Fontainebleau, France and is a Certified Public Accountant (inactive). We believe that Mr. Modig's extensive international experience in finance and operations, private equity, and mergers and acquisitions qualifies him to serve on the Board.

Senthil Sundaram

Mr. Sundaram has served as a member of the Board since June 2019. In July 2020, Mr. Sundaram became the Chief Executive Officer and a director of Terns Pharmaceuticals, Inc., a publicly-traded clinical-stage pharmaceutical company. Mr. Sundaram served as the Chief Financial Officer of Nightstar Therapeutics plc, a publicly-traded clinical-stage gene therapy company, from April 2017 to June 2019, when it was acquired by Biogen, Inc., a multinational biotechnology company. While at Nightstar, Mr. Sundaram led a number of private and public offerings, including its initial public offering, and a variety of business development efforts including the M&A process that resulted in the acquisition by Biogen. From February 2013 to April 2017, Mr. Sundaram served in a variety of positions at Intercept Pharmaceuticals, Inc., a biopharmaceutical company, including most recently as its Vice President and head of business development. Prior to joining Intercept, from 2000 to 2013, Mr. Sundaram worked in the healthcare investment banking groups at Lehman Brothers Inc., Barclays Capital Inc., Citigroup Global Markets Inc. and Lazard Ltd. Mr. Sundaram earned a B.S. in Computer Engineering and a B.A. in Economics from Brown University. We believe that Mr. Sundaram's extensive experience in leadership roles at biopharmaceutical companies qualifies him to serve on the Board.

Eric Venker, M.D., Pharm.D.

Dr. Venker has served as a member of the Board since February 2020. Since February 2021, Dr. Venker has served as President, Chief Operating Officer of RSI, having previously served as Chief Operating Officer of RSI since November 2018 and as President of RSI since January 2021. From October 2017 to October 2018, Dr. Venker served as Chief of Staff to RSI's Chief Executive Officer, and from 2014 to 2015 as an Analyst at RSI. From 2015 to 2017, Dr. Venker was a physician at New York Presbyterian Hospital/Columbia University Medical Center, where he trained in internal medicine, and also served as Chair of the Housestaff Quality Council leading operational initiatives to improve efficiencies. From 2011 to 2015, Dr. Venker was a Clinical Pharmacist at Yale-New Haven Hospital. Dr. Venker also serves on the boards of directors of Arbutus Biopharma Corporation and Immunovant, Inc., each a biopharmaceutical company, as well as several private biopharmaceutical companies. Dr. Venker received his Pharm.D. from St. Louis College of Pharmacy and his M.D. from Yale School of Medicine. We believe that Dr. Venker's medical background and experience in the biopharmaceutical industry qualify him to serve on the Board.

Kristiina Vuori, M.D., Ph.D.

Dr. Vuori has served as a member of the Board since October 2020. Dr. Vuori has served as President of Sanford Burnham Prebys Medical Discovery Institute, or the Institute, since January 2010. The Institute is a non-profit research organization focused on biomedical research and drug discovery in the areas of cancer, neurodegeneration, diabetes, and infectious, inflammatory, and childhood diseases. In addition, Dr. Vuori has held the Pauline and Stanley Foster Presidential Chair since January 2010 and has served as Professor at the Institute since January 1995. From July 2014 to September 2017, Dr. Vuori served on the board of directors of WebMD Health Corp., an online publisher of health news and information, and since June 2019, has served on the board of directors of Bionano Genomics, Inc., a life sciences instrumentation company. She has served on the board of directors of Forian, Inc., a health data analytics company, since January 2021. Additionally, she serves or has served in the past five years on the boards of directors of the American Association for Cancer Research and the California Institute for Regenerative Medicine. Dr. Vuori earned her M.D. and Ph.D. from the University of Oulu, Finland. We believe that that Dr. Vuori's experience as a physician-scientist in biomedical research and drug discovery and as an educator of research scientists, her experience managing a large non-profit research organization, and her various leadership roles in non-profit, for-profit and public boards qualify her to serve on the Board.

Executive Officers

The following table sets forth information concerning our executive officers and other senior management, including their ages, as of April 30, 2021:

Name	Age	Position[(1)]
Executive Officers		
Pavan Cheruvu, M.D.	39	Chief Executive Officer
David Nassif, J.D.	67	Chief Financial Officer and Chief Accounting Officer, General Counsel
Gavin Corcoran, M.D.	58	Chief R&D Officer

Executive Officers

Pavan Cheruvu, M.D.

See "Directors, Executive Officer's and Corporate Governance—Pavan Cheruvu, M.D."

David Nassif, J.D.

Mr. Nassif served as the Principal Financial and Accounting Officer, General Counsel of Axovant Gene Therapies Ltd. from July 2019 until November 2020 and as the Chief Financial Officer of Axovant Sciences, Inc. from July 2019 through December 2020, and has served as the Chief Financial Officer and Chief Accounting Officer, General Counsel of Sio Gene Therapies Inc. since November 2020. He served as Executive Vice President and Chief Financial Officer of SteadyMed, Ltd., a specialty pharmaceutical company, from March 2013 (first as a financial consultant and commencing March 2015 on a full-time basis) until June 2019. From May 2011 through September 2014, Mr. Nassif served as the President and Chief Financial Officer of Histogen, Inc., a regenerative medicine company. From May 2007 to February 2010, Mr. Nassif served as the Executive Vice President and Chief Financial Officer of Zogenix, Inc., a specialty pharmaceutical company. Mr. Nassif received a B.Sc. in Finance and Management Information Systems from the University of Virginia with honors and a J.D. from the University of Virginia School of Law.

Gavin Corcoran, M.D.

Dr. Corcoran has served as our Chief R&D Officer since November 2020 and served as the Chief R&D Officer of Axovant Sciences, Inc. from July 2018 until December 2020. Prior to joining Axovant, he served as Chief Medical Officer of Allergan plc from March 2015 to June 2018 and of Actavis plc from July 2014 to March 2015. Dr. Corcoran served as Executive Vice President for Global Medicines Development at Forest Laboratories from December 2011 to June 2014, prior to the acquisition of Forest Laboratories, Inc. by Actavis in 2014. Earlier in his career, Dr. Corcoran also served as Head of Late Stage Clinical Development for Inflammation and Immunology at Celgene Corporation, Chief Scientific Officer and head of R&D at Stiefel Laboratories and he held various leadership roles in clinical development and regulatory affairs at Amgen Inc., Schering-Plough Corporation, and Bayer AG. He received his M.B.B.Ch. from the University of the Witwatersrand in South Africa and completed his clinical training in internal medicine and infectious diseases at the University of Texas Health Science Center at San Antonio.

Information Regarding the Board of Directors and Corporate Governance

Board Leadership Structure

Dr. Torti currently serves as Chairperson of the Board. The Board believes that Dr. Torti's role as Chairperson helps ensure that management and the Board act with common purpose and benefit from the extensive executive leadership and operational experience of Dr. Torti. The Board believes that Dr. Torti is well-positioned to act as a bridge between management and the Board, facilitating the regular flow of information. In addition, the Board believes that, under current circumstances, the separation of the offices of Chairperson and Chief Executive Officer will enhance oversight of management and Board function, allowing Dr. Cheruvu the ability to focus on his primary responsibilities as Chief Executive Officer, enhancing shareholder value and expanding and strengthening our business.

Our corporate governance guidelines provide that the Board will select its Chairperson in the manner that it determines to be in the best interests of our shareholders. The same person may hold the positions of Chief Executive Officer and Chairperson, or the Board may separate these offices. If the Chairperson is an independent director, the Board may designate the Chairperson as the lead independent director. If the Chairperson is not an independent director, the Board may designate one of the independent directors as the lead independent director. Dr. Pande was designated by the Board as our lead independent director in September 2018. The lead independent director's duties include among other things: establishing the agenda for meetings of the independent directors and meetings of the non-management directors, as applicable; presiding over meetings of the independent directors and meetings of the non-management directors, as applicable; presiding over any portions of meetings of the Board evaluating the performance of the Board; and coordinating the activities of the other independent directors and perform such other duties the Board may establish or delegate.

At the present time, the Board believes that the current Board members, together with our management, possess the requisite leadership and industry skills, expertise and experiences to effectively oversee our business and affairs. Moreover, the Board prefers to retain the flexibility to select the appropriate leadership structure based upon the existence of various conditions, including, but not limited to, business, financial or other market conditions, affecting us at any given time. Notwithstanding the foregoing, the independent directors of the Board regularly participate in executive sessions at which only independent directors are present.

Role of the Board in Risk Oversight

One of the Board's key functions is informed oversight of our risk management process. The Board administers this oversight function directly through the Board as a whole, as well as through various Board standing committees that address risks inherent in their respective areas of oversight. The Board believes its current leadership structure, including the appointment of a lead independent director and having a majority or equal number of independent directors on each committee and the Board itself, supports the risk oversight function of the Board.

In particular, the Board is responsible for reviewing, approving and monitoring fundamental financial and business strategies and major corporate actions, assessing major risks facing us and considering ways to address those risks and overseeing the establishment and maintenance of processes and conditions to maintain our integrity. Our Board has received regular updates from the management team on the evolving COVID-19 situation and is involved in strategy decisions related to the impact of COVID-19 on our business. The Audit Committee of the Board has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. The Audit Committee of the Board also monitors compliance with certain legal and regulatory requirements, including oversight of related-person transactions, complaint procedures, certain ethical compliance and regulatory and accounting initiatives, and is responsible for oversight of the performance of our internal audit function. The Compensation Committee of the Board assesses and monitors whether any of our compensation policies and programs have the potential to encourage excessive risk-taking. The Nominating and Corporate Governance Committee of the Board monitors the effectiveness of our corporate governance guidelines, including whether they are successful in preventing illegal or improper liability-creating conduct, and monitor compliance with certain regulatory requirements. It is the responsibility of the committee chairs to report findings regarding material risk exposures to the Board as quickly as possible.

The oversight responsibility of the Board and its committees is informed by reports from our management team that are designed to provide visibility to Board about the identification and assessment of key risks and our risk mitigation strategies. At periodic meetings of the Board and its committees, management reports to and seeks guidance from the Board and its committees with respect to the most significant risks that could affect our business, such as legal risks, information security and privacy risks, and financial, tax and audit related risks. In addition, among other matters, management provides the Audit Committee and Nominating and Corporate Governance Committee of the Board periodic reports on our compliance programs and investment policy and practices.

Meetings of the Board of Directors; Attendance at Annual Meeting of Shareholders

During our fiscal year ended March 31, 2021, the Board met 7 times; the Audit Committee met four times; the Compensation Committee met two times; and the Nominating and Corporate Governance Committee met three times. Each Board member attended 75% or more of the aggregate number of meetings of the Board and of the committees on which he or she served that were held during the portion of the last fiscal year for which he or she was a director or committee member.

As required under applicable Nasdaq listing rules, in our fiscal year ended March 31, 2021, our independent directors met in regularly scheduled executive sessions at which only independent directors were present. Dr. Pande and Mr. Modig typically presided over the executive sessions.

Our policy is that directors are invited to attend the Annual General Meetings of Shareholders. No members of the Board attended our 2020 Annual General Meeting of Shareholders.

Information Regarding Committees of the Board of Directors

The Board has an Audit Committee, a Compensation Committee and a Nominating and Corporate Governance Committee. Below is a description of each of these committees. Each committee has the authority to engage legal counsel or other experts or consultants, as it deems appropriate to carry out its responsibilities. Copies of the written charters of such committees, are available on our website at http://investors.siogtx.com/investors/corporate-governance. Information contained on or accessible through this website is not incorporated by reference nor otherwise included in this report, and any references to this website are intended to be inactive textual references only.

As previously disclosed, on February 24, 2020, we completed a public offering of our shares of common stock and pre-funded warrants to purchase shares of common stock, which resulted in Roivant Sciences Ltd. ("RSL") no longer controlling a majority of the voting power of our outstanding shares of common stock (the "February Offering"). As a result of the February Offering, we no longer qualify as a "controlled company" for purposes of certain exemptions from the corporate governance standards of Nasdaq, including director independence.

Audit Committee

The Audit Committee of the Board was established by the Board in accordance with Section 3(a)(58)(A) of the Exchange Act to oversee our corporate accounting and financial reporting processes and audits of our financial statements. The Board reviews Nasdaq listing standards definition of independence for Audit Committee members on an annual basis and has determined that each member of the Audit Committee satisfies the independence requirements under applicable Nasdaq listing rules and Rule 10A-3 of the Exchange Act.

The Audit Committee is composed of Mr. Modig, Dr. Pande and Mr. Sundaram. The Board has also determined that each of Mr. Modig and Mr. Sundaram qualifies as an "audit committee financial expert," as defined in applicable Securities and Exchange Commission ("SEC") rules and regulations. The Board made a qualitative assessment of Mr. Modig's level of knowledge and experience based on a number of factors, including his formal education and experience as a chief financial officer at public reporting companies. In addition to our Audit Committee, Mr. Modig also serves on the audit committees of two other public companies, Kiadis Pharma N.V. and Affimed N.V. Likewise, the Board made a qualitative assessment of Mr. Sundaram's level of knowledge and experience based on a number of factors, including his experience as a chief financial officer at a public reporting company and investment banker. The Board has determined that this simultaneous service of Mr. Modig does not impair his ability to effectively serve on our Audit Committee.

The principal duties and responsibilities of the Audit Committee include:

- recommending and retaining an independent registered public accounting firm to serve as our independent auditors, for purposes of the Companies Act, overseeing our independent auditors' work and determining our independent auditors' compensation;
- evaluating the performance of and assessing the qualifications of our independent auditors;
- approving in advance all audit services and non-audit services to be provided to us by our independent auditors;
- monitoring the rotation of partners of the independent auditors on our audit engagement team as required by law;
- assessing and taking other appropriate action to oversee the independence of our independent auditors, including reviewing written disclosures from the independent auditors delineating all relationships between the auditors, or their affiliates, and us, or persons in financial oversight roles at Sio, that may reasonably be thought to bear on independence (at least annually, consistent with the Public Company Accounting Oversight Board, or PCAOB, Rule 3526);
- reviewing the financial statements proposed to be included in our Annual Report on Form 10-K to be filed with the SEC and recommending to the Board whether such financial statements should be so included;
- reviewing and discussing with management and our independent auditors the results of the annual audit and the independent auditor's review of our quarterly financial statements, including, as appropriate, a review of our disclosures under "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our periodic reports filed with the SEC;
- reviewing and discussing with management and our independent auditors, as appropriate, our guidelines and policies with respect to risk assessment and management, including risks related to our accounting matters, financial reporting and legal and regulatory compliance; and reviewing and discussing with management, as appropriate, insurance programs;
- conferring with management and our independent auditors, as appropriate, regarding the scope, adequacy and effectiveness of our internal control over financial reporting;
- coordinating the Board's oversight of the performance of our internal audit function;
- reviewing and approving or rejecting transactions between us and any related persons; and
- establishing procedures for the receipt, retention and treatment of complaints received by us regarding accounting, internal accounting controls, auditing or compliance matters and the confidential and anonymous submission by our employees of concerns regarding questionable accounting or auditing matters.

Report of the Audit Committee of the Board of Directors*

The Audit Committee has reviewed and discussed the audited financial statements for our fiscal year ended March 31, 2021 with our management. The Audit Committee has discussed with the independent registered public accounting firm the matters required to be discussed by Auditing Standard No. 1301, Communications with Audit Committees, as adopted by the PCAOB. The Audit Committee has also received the written disclosures and the letter from the independent registered public accounting firm required by applicable requirements of the PCAOB regarding the independent accountants' communications with the Audit Committee concerning independence, and has discussed with the independent registered public accounting firm the accounting firm's independence. Based on the foregoing, the Audit Committee has recommended to the Board that the audited financial statements be included in our Annual Report on Form 10-K for our fiscal year ended March 31, 2021.

Mr. Senthil Sundaram
Mr. Berndt Modig
Dr. Atul Pande

* *The material in this report is not deemed "filed" with the SEC, and is not to be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.*

Compensation Committee

The Compensation Committee is composed of Mr. Modig and Dr. Pande. The Board has determined that Mr. Modig and Dr. Pande are "independent," as independence is currently defined in applicable Nasdaq listing rules. All members of the Compensation Committee are "non-employee directors," as defined in Rule 16b-3 under the Exchange Act.

The Compensation Committee of the Board acts on behalf of the Board to, among other things, oversee our compensation strategy, policies, plans and programs and to review and determine the compensation to be paid to our executive officers. In general, the Compensation Committee of the Board performs the same policy- and compensation-setting functions for our subsidiaries and their executive officers as it does for us, and references herein to our personnel, policies, plans and programs include those of our subsidiaries as well. The principal duties and responsibilities of the Compensation Committee include:

- reviewing, modifying and approving our overall compensation strategy and policies, including: (1) reviewing and approving corporate goals and objectives relevant to the compensation of our executive officers and other senior management, as appropriate; (2) evaluating and approving, or recommending to the Board for approval, compensation plans and programs advisable for us, including modifications and terminations to those plans and programs; (3) establishing policies with respect to equity compensation arrangements; (4) assessing the adequacy and competitiveness of our executive compensation programs among comparable companies in our industry; (5) reviewing and approving the terms of any employment agreements, severance arrangements, change-of-control protections and any other compensatory arrangement for our executive officers and other senior management, as appropriate; (6) reviewing our practices and policies of employee compensation as they relate to risk management and risk-taking incentives; (7) considering and establishing share ownership guidelines for our executive officers and directors, if deemed appropriate; and (8) evaluating the efficacy of our compensation policy and strategy in achieving expected benefits to us and otherwise furthering our policies;

- establishing and approving individual and corporate goals and objectives of our Chief Executive Officer and our other executive officers and senior management and evaluating performance of the Chief Executive Officer and our other executive officers and senior management, as appropriate, in light of these stated objectives;

- reviewing and approving the type and amount of compensation to be paid or awarded to Board members;

- selecting and retaining compensation consultants, legal counsel and other advisers; and

- adopting, amending, administering, and terminating our equity compensation plans, pension and profit sharing plans, bonus plans, deferred compensation plans and similar programs.

Compensation Committee Processes and Procedures

The Compensation Committee meets at least once annually and with greater frequency if necessary. The agenda for each meeting is usually developed by the Chairperson of the Compensation Committee, in consultation with the Chief Executive Officer and the General Counsel. The Compensation Committee meets regularly in executive session. From time to time, various members of management and other employees as well as outside advisors or consultants may be invited by the Compensation Committee to make presentations, to provide financial or other background information, to provide advice or to otherwise participate in Compensation Committee meetings. The Chief Executive Officer may not participate in, or be present during, the voting or deliberations of the Compensation Committee regarding his compensation. The charter of the Compensation Committee grants the Compensation Committee full access to all books, records, facilities and personnel of Sio.

In addition, under the charter, the Compensation Committee has the authority to obtain, at our expense, advice and assistance from internal or external legal, accounting or other advisors and consultants that any member of the Compensation Committee deems necessary or appropriate in the discharge of his or her responsibilities. If the Compensation Committee chooses to retain or obtain the advice of a compensation consultant, independent legal counsel, or other advisor, it has the direct responsibility for the appointment, compensation and oversight of the work of such party, and we will provide for appropriate funding, as determined by the Compensation Committee, for the payment to such party. In addition, the Compensation Committee has the sole authority to retain and terminate any compensation consultant to assist in its evaluation of executive and director compensation, including the sole authority to approve the consultant's reasonable fees and other retention terms, all at our expense. Under the charter, the Compensation Committee may select a compensation consultant, legal counsel or other advisor (other than in-house legal counsel and certain other types of advisors) only after taking into consideration all factors relevant to that party's independence from management, including the six factors prescribed by the SEC and Nasdaq; however, there is no requirement that any advisor be independent.

During the past fiscal year, after taking into consideration the six factors prescribed by the SEC and Nasdaq, the Compensation Committee engaged Radford, a national compensation consulting firm, to provide executive compensation advisory services based, in part, on its reputation and extensive experience in the industry. The Compensation Committee determined that Radford was independent from management and had no conflicts of interest in connection with the advisory services to be provided. Specifically, the Compensation Committee requested that Radford develop a comparative group of companies and perform analyses of competitive performance and compensation levels for that group. Radford has also conducted interviews with members of the Compensation Committee and senior management to learn more about our business operations and strategy, key performance metrics and strategic goals, as well as the labor markets in which we compete. Radford ultimately developed recommendations that were presented to the Compensation Committee for its consideration. Following an active dialogue with Radford, the Compensation Committee approved the recommendations.

The Compensation Committee generally makes adjustments to annual compensation, determines bonuses and equity awards and establishes new performance objectives at one or more meetings held during the first quarter of the year. However, the Compensation Committee also considers matters related to individual compensation, such as compensation for new executive hires, as well as high-level strategic issues, such as the efficacy of our compensation strategy, potential modifications to that strategy and new trends, plans or approaches to compensation, at various meetings throughout the year.

Generally, the Compensation Committee's process comprises two related elements: the determination of compensation levels and the establishment of performance objectives for the current year. For executives other than the Chief Executive Officer, the Compensation Committee solicits and considers evaluations and recommendations submitted to the Compensation Committee by the Chief Executive Officer. The evaluation of the performance of the Chief Executive Officer is conducted by the Compensation Committee, which determines any adjustments to his compensation as well as awards to be granted. For all executives and directors, the Compensation Committee may review and consider, as appropriate, materials such as financial reports and projections, operational data, tax and accounting information, tally sheets that set forth the total compensation that may become payable to executives in various hypothetical scenarios, executive and director share ownership information, company share performance data, analyses of historical executive compensation levels and current company-wide compensation levels and recommendations of the Compensation Committee's compensation consultant, including analyses of executive and director compensation paid at other companies identified by the consultant.

Nominating and Corporate Governance Committee

The Nominating and Corporate Governance Committee is composed of Dr. Pande, Mr. Sundaram and Dr. Vuori. The Board has determined that Dr. Pande, Mr. Sundaram and Dr. Vuori are "independent," as independence is currently defined in applicable Nasdaq listing rules. The principal duties and responsibilities of the Nominating and Corporate Governance Committee include:

- identifying, reviewing and evaluating candidates to serve as directors, consistent with criteria approved by the Board;
- reviewing, evaluating and considering the recommendation for nomination of incumbent directors for re-election to the Board;
- reviewing, discussing and assessing the performance of the Board, including Board committees, such assessment to include evaluation of the Board's contribution as a whole and effectiveness in serving the best interests of Sio and its shareholders, specific areas in which the Board and/or management believe contributions could be improved, overall Board composition and makeup, including the reelection of current Board members, and the independence of directors;
- overseeing the Board's committee structure and operations, evaluating the performance of the members of the committees of the Board, reviewing the composition of such committees, and recommending to the Board the membership of each such committee;
- reviewing, discussing and assessing our corporate governance principles;
- reviewing our policy statements to determine adherence to our Code of Business Ethics and Conduct; and
- overseeing and reviewing the processes and procedures we use to provide accurate, relevant and appropriately detailed information to the Board and its committees on a timely basis.

The Nominating and Corporate Governance Committee believes that candidates for director should have certain minimum qualifications, including the ability to read and understand basic financial statements, being over 21 years of age and having the highest personal integrity and ethics. The Nominating and Corporate Governance Committee also intends to consider such factors as possessing relevant expertise upon which to be able to offer advice and guidance to management, having sufficient time to devote to the affairs of Sio, demonstrated excellence in his or her field, having the ability to exercise sound business judgment, diversity and having the commitment to rigorously represent the long-term interests of our shareholders. However, the Nominating and Corporate Governance Committee retains the right to modify these qualifications from time to time. Candidates for director nominees are reviewed in the context of the current composition of the Board, our operating requirements and the long-term interests of our shareholders. In conducting this assessment, the Nominating and Corporate Governance Committee typically considers diversity, age, skills and such other factors as it deems appropriate, given the current needs of the Board and Sio, to maintain a balance of knowledge, experience and capability.

In the case of incumbent directors whose terms of office are set to expire, the Nominating and Corporate Governance Committee reviews these directors' overall service to us during their terms, including the number of meetings attended, level of participation, quality of performance and any other relationships and transactions that might impair the directors' independence. The Nominating and Corporate Governance Committee also takes into account the results of the Board's self-evaluation, conducted annually on a group and individual basis.

In the case of new director candidates, the Nominating and Corporate Governance Committee also determines whether the nominee is independent for Nasdaq purposes, which determination is based upon applicable Nasdaq listing standards, applicable SEC rules and regulations and the advice of counsel, if necessary. The Nominating and Corporate Governance Committee then uses its network of contacts to compile a list of potential candidates, but may also engage, if it deems appropriate, a professional search firm. The Nominating and Corporate Governance Committee conducts any appropriate and necessary inquiries into the backgrounds and qualifications of possible candidates after considering the function and needs of the Board. The Nominating and Corporate Governance Committee meets to discuss and consider the candidates' qualifications and then selects a nominee for recommendation to the Board by majority vote.

The Nominating and Corporate Governance Committee will consider director candidates recommended by shareholders. The Nominating and Corporate Governance Committee does not intend to alter the manner in which it evaluates candidates, including the minimum criteria set forth above, based on whether or not the candidate was recommended by a shareholder.

Shareholder Communications with the Board of Directors

The Board has adopted a formal process by which shareholders may communicate with the Board or any of its directors. Shareholders who wish to communicate with the Board or an individual director may do so by sending written communications to the Board or such director at Sio Gene Therapies Inc., Attn: Corporate Secretary, at 130 West 42nd Street, 26th Floor, New York, New York 10036. The Corporate Secretary will forward each communication to the Legal Department of Sio Gene Therapies Inc., and the communication will be further forwarded to the Board or individual directors to whom the communication is addressed unless the communication contains advertisements or solicitations or is unduly hostile, threatening or similarly inappropriate, in which case the communication will be discarded.

In addition to shareholder communications with directors, any interested person may communicate directly with the presiding director of the Board's executive sessions or the independent or non-management directors as a group. Persons interested in communicating directly with the independent or non-management directors regarding their concerns or issues may do so by addressing correspondence to a particular director, or to the independent or non-management directors generally, in care of Sio Gene Therapies Inc., Attn: Corporate Secretary, at 130 West 42nd Street, 26th Floor, New York, New York 10036. If no particular director is named, letters will be forwarded, depending upon the subject matter, to the Chairperson of the Audit, Compensation, or Nominating and Corporate Governance Committee.

Please note that the foregoing communication procedure does not apply to (i) shareholder proposals pursuant to Exchange Act Rule 14a-8 and communications made in connection with such proposals or (ii) service of process or any other notice in a legal proceeding.

Code of Business Ethics and Conduct

The Board has adopted a Code of Business Ethics and Conduct, or Code of Conduct, that applies to all of our directors, officers, employees, consultants and independent contractors. The Code of Conduct is available on our website at http://investors.siogtx.com/investors/corporate-governance. Information contained on or accessible through this website is not incorporated by reference nor otherwise included in this report, and any references to this website are intended to be inactive textual references only. If we make any substantive amendments to the Code of Conduct or grant any waiver from a provision of the Code of Conduct to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website or otherwise as required by applicable law and Nasdaq listing requirements.

Corporate Governance Guidelines

The Board has adopted Corporate Governance Guidelines to establish the authority and practices to review and evaluate our business operations as needed and to make decisions that are independent of our management. The guidelines are also intended to align the interests of directors and management with those of our shareholders. The Corporate Governance Guidelines set forth the practices that the Board intends to follow with respect to a number of areas, including its composition and selection, role, meetings, committees, access to management and use of outside advisors, Chief Executive Officer evaluation and succession planning, and Board assessment and compensation. The Corporate Governance Guidelines may be viewed at http://investors.siogtx.com/investors/corporate-governance. Information contained on or accessible through this website is not incorporated by reference nor otherwise included in this report, and any references to this website are intended to be inactive textual references only.

Item 11. Executive Compensation

Summary Compensation Table

The following table sets forth, for our fiscal years ended March 31, 2021 and 2020, compensation awarded or paid to, or earned by, our principal executive officer and our two next most highly compensated executive officers as of March 31, 2021. These executive officers are referred to herein as our named executive officers.

Name and Principal Position	Fiscal Year	Salary	Stock Awards [1]	Option Awards[1]	Non-Equity Incentive Plan Compensation[2]	Other	Total
Pavan Cheruvu, M.D.	2020	$ 517,500	$388,815	$ 483,113	$ 298,080	$ 19,191 [3]	$ 1,706,699
Chief Executive Officer	2019	500,000	351,056	1,784,077	225,000	8,616 [4]	2,868,749
David Nassif, J.D. [5]	2020	414,000	181,470	225,415	213,728	43,485 [6]	1,078,098
Chief Financial Officer and Chief Accounting Officer, General Counsel	2019	300,000	234,032	970,828	175,000	81,350 [7]	1,761,210
Gavin Corcoran, M.D. [7]	2020	433,500	146,280	181,989	204,769	17,410 [8]	983,948
Chief R&D Officer	2019	425,000	248,663	628,885	146,094	8,616	1,457,258

[1] Amounts reported in this column do not reflect the amounts actually received by our named executive officers. Instead, these amounts reflect the aggregate grant date fair value of each stock option and stock award granted to the named executive officers during the indicated fiscal year, as computed in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 718. Assumptions used in the calculation of these amounts are included in Note 10 to our consolidated financial statements included in this Annual Report on Form 10-K for the year ended March 31, 2021. As required by SEC rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions. In March 2020, RSL forfeited all of Dr. Cheruvu's RSL restricted stock units ("RSL RSUs") and granted him newly issued RSL equity instruments: RSL performance options and RSL capped value appreciation rights ("RSL CVARs"). The vesting of the RSL performance options and RSL CVARs is not deemed probable as of March 31, 2021. These two instruments will vest only to the extent certain RSL liquidity conditions and vesting requirements (a mix of time-based and market conditions) are achieved by a specified date in the future, and provided, for the time-based vesting requirements, that Dr. Cheruvu has provided continued service to RSL or an affiliate of RSL, such as Sio. As a result, as of the grant date the RSL performance options and RSL CVARs performance criteria were deemed not probable of occurring, therefore no stock-based compensation expense has been recorded related to these newly awarded RSL instruments and no value has been ascribed to such instruments in the table above. Assuming that the vesting conditions to the RSL performance options and RSL CVARs were met and the performance criteria was deemed probable, the value of such awards as of the grant date would have been $7.7 million.

[2] See "—Annual Cash Bonus".

[3] Amount includes (a) $18,975 in 401(k) matching contributions.

[4] Amount excludes $1,011,993 in stock-based compensation expense allocated to Sio from RSL for RSL equity instruments granted to Dr. Cheruvu.

[5] Mr. Nassif joined Sio in July 2019.

[6] Amount includes (a) $25,173 for reimbursed temporary housing expenses, as a result of the Company requiring Mr. Nassif to reside in New York City for one year as a condition to his employment; and (b) $18,172 in 401(k) matching contributions.

[7] Amount includes (a) $78,206 for reimbursed temporary housing expenses.

[8] Amount includes (a) $17,194 in 401(k) matching contributions.

Narrative to Summary Compensation Table

We review compensation annually for all employees, including our named executive officers. In setting executive base salaries and bonuses and granting equity incentive awards, we consider compensation for comparable positions in the market, the historical compensation levels of our executives, individual performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders and a long-term commitment to Sio. We do not target a specific competitive position or a specific mix of compensation among base salary, bonus or long-term incentives.

The Compensation Committee of the Board has historically determined compensation for our named executive officers. The Compensation Committee typically reviews and discusses management's proposed compensation with the Chief Executive Officer for all named executive officers other than the Chief Executive Officer. Based on those discussions and its discretion, the Compensation Committee then recommends the compensation for each named executive officer. The Compensation Committee, without members of management present, discusses and ultimately approves the compensation of our named executive officers. For our fiscal years ended March 31, 2021 and 2020, the Compensation Committee retained Radford, a compensation consulting firm, to evaluate and make recommendations with respect to our executive compensation program.

Annual Cash Bonus

We seek to motivate and reward our executives for achievements relative to our corporate goals and expectations for each fiscal year. For the fiscal year ending March 31, 2022, the target cash bonus for Dr. Cheruvu is 60% of his base salary, subject to the achievement of overall company performance criteria, and the target cash bonus for each of Mr. Nassif and Mr. Corcoran is 50% of their respective base salaries, subject to the achievement of individual performance criteria to be determined by the Board or the Compensation Committee, as well as overall company performance criteria.

Additionally, On March 30, 2021, the Compensation Committee of the Board approved a one-time cash performance incentive for Dr. Corcoran (the "Performance Incentive"). Under the terms of the Performance Incentive, Dr. Corcoran shall be paid a bonus of $35,000 upon completion of patient enrollment in the dose-escalation Stage 1 of our AXO-AAV-GM1 gene therapy program for the treatment of GM1 gangliosidosis, including both Type 1 (early infantile) and Type 2 (late infantile and juvenile) patients if such enrollment occurs on or before March 31, 2022. Additionally, Dr. Corcoran shall be paid a bonus of $35,000 upon dosing of the first patient in our AXO-Lenti-PD gene therapy program for the treatment of Parkinson's disease using clinical trial material from a suspension-based manufacturing process if such dosing occurs on or before March 31, 2022.

For the years ended March 31, 2021 and March 31, 2020, bonuses were awarded based on our achievement of specified corporate goals, including creating value with our gene therapy pipeline and finance goals, as well as individual goals for the named executive officers. Dr. Cheruvu's bonuses were weighted 100% based on the achievement of corporate goals. For each other named executive officer, the bonuses were weighted 75% based on the achievement of the corporate goals and 25% based on the achievement of individual objectives established for each such officer. In March 2020, the Compensation Committee awarded each named executive officer a bonus for the year ended March 31, 2020, based on each named executive officer's achievement of corporate goals at the 75% level and individual goals at levels ranging from 50% to 125%. In March 2021, the Compensation Committee awarded each named executive officer a bonus for the year ended March 31, 2021, based on each executive officer's achievement of corporate goals at the 96% level and individual goals at levels ranging from 90% to 125%.

Outstanding Equity Awards as of March 31, 2021

The following table shows certain information regarding outstanding equity awards held by our named executive officers as of March 31, 2021, as adjusted to reflect the 1-for-8 reverse stock split effected in May 2019. All option awards were granted under our 2015 Amended and Restated Equity Incentive Plan.

	Option Awards				Restricted Stock Units (RSUs)		
Name	Number of Securities Underlying Unexercised Options Exercisable [1]	Number of Securities Underlying Unexercised Options Unexercisable [2][3]	Option Exercise Price	Option Expiration Date	Number of Vested Securities Underlying	Number of Unvested Securities Underlying [4]	Market Value of Outstanding RSUs [5]
Pavan Cheruvu, M.D.[6]	6,250	—	$ 127.92	11/15/2025	—	—	—
	6,250	—	193.92	4/27/2027	—	—	—
	181,894	60,629	14.48	2/12/2028	—	—	—
	—	199,500 [7]	8.48	4/14/2029	—	—	—
	87,282	112,218	8.48	4/14/2029	—	—	—
	—	169,100	3.45	4/14/2030	—	—	—
	—	—	—	—	—	112,700	$ 294,147
David Nassif, J.D.	—	75,000 [8]	6.42	6/30/2029	—	—	—
	56,250	93,750	6.42	6/30/2029	—	—	—
	—	78,900	3.45	4/14/2030	—	—	—
	—	—	—	—	—	52,600	137,286
Gavin Corcoran, M.D.	—	25,000 [9]	19.68	7/15/2028	—	—	—
	19,537	11,713	19.68	7/15/2028	—	—	—
	—	25,000 [7]	8.48	4/14/2029	—	—	—
	41,948	53,927	8.48	4/14/2029	—	—	—
	—	63,700	3.45	4/14/2030	—	—	—
	—	—	—	—	—	42,400	110,664

(1) Because options granted to the named executive officers are exercisable immediately subject to a repurchase right in our favor which lapses as the option vests, this column reflects the number of options held by the named executive officers that were exercisable and vested as of March 31, 2021.

(2) Because options granted to the named executive officers are exercisable immediately subject to a repurchase right in our favor which lapses as the option vests, this column reflects the number of options held by the named executive officers that were exercisable and unvested as of March 31, 2021.

(3) Except as otherwise noted, each of these options vests as to 25% of the underlying shares of common stock one year from the date of grant, with the remaining shares of common stock vesting in 12 equal quarterly installments thereafter, provided the named executive officer has provided continuous service to us through each such date. All shares of common stock underlying each of these options will become fully vested upon a change in control, as that term is defined in our Amended and Restated 2015 Equity Incentive Plan.

(4) These unvested restricted shares are scheduled to vest in three equal annual installments on the first, second and third anniversaries of the date of grant, provided the named executive officer has provided continuous service to us through that date.

(5) The market value is equal to the product of $2.61, which is the closing price of our common stock on March 31, 2021, and the sum of the number of vested and unvested RSUs.

(6) Excludes all RSL equity instruments. RSL granted RSL awards, RSL vanilla options and RSL RSUs to Dr. Cheruvu while he was employed by RSL's subsidiary, Roivant Sciences, Inc., prior to his commencement of employment as our Chief Executive Officer. In March 2020, RSL purchased a portion of Dr. Cheruvu's RSL awards and RSL vanilla options, and all of Dr. Cheruvu's RSL RSUs were forfeited, in exchange for $1.2 million in cash and two newly issued RSL equity instruments. The vesting of these two RSL equity instruments, RSL performance options and RSL CVARs, is not deemed probable as of March 31, 2021. These two instruments will vest only to the extent certain RSL liquidity conditions and vesting requirements (a mix of time-based and market conditions) are achieved by a specified date in the future, and provided, for the time-based vesting requirements, that Dr. Cheruvu has provided continued service to RSL or an affiliate of RSL, such as Sio. The RSL vanilla options are subject to specified time-based vesting schedules and requirements, provided that Dr. Cheruvu has provided continuous service to RSL or an affiliate of RSL, such as Sio, through such date. The RSL awards are fully vested as of March 31, 2021. The aggregate fair value of the RSL equity instruments held by Dr. Cheruvu was $3.6 million at March 31, 2021. Significant judgment and estimates were used to estimate the fair value of these RSL equity instruments, as they are not publicly traded.

(7) One-third of the option will vest at such time as the Company's stock price is equal to or greater than $16.96 per share, one-third of the option will vest at such time as the Company's stock price is equal to or greater than $33.92 per share, and one-third of the option will vest at such time as the Company's stock price is equal to or greater than $50.88 per share, provided the named executive officer has provided continuous service to us through each such date.

(8) One-third of the option will vest at such time as the Company's stock price is equal to or greater than $12.84 per share, one-third of the option will vest at such time as the Company's stock price is equal to or greater than $25.68 per share, and one-third of the option will vest at such time as the Company's stock price is equal to or greater than $38.52 per share, provided the named executive officer has provided continuous service to us through each such date.

(9) One-third of the option will vest at such time as the Company's stock price is equal to or greater than $59.04 per share, one-third of the option will vest at such time as the Company's stock price is equal to or greater than $98.40 per share, and one-third of the option will vest at such time as the Company's stock price is equal to or greater than $137.76 per share, provided the named executive officer has provided continuous service to us through each such date.

Employment, Severance and Change in Control Agreements

The employment agreement or offer letter for each of our named executive officers sets forth the initial terms and conditions of his employment. These agreements provide for at-will employment and set forth the officer's annual base salary, performance bonus target opportunity, initial equity incentive grant, terms of severance and eligibility for employee benefits. Each of them provided services to us pursuant to one or more inter-company services agreements between Axovant Gene Therapies Ltd. and its wholly owned subsidiaries until August 2020. For the purposes of this discussion, references to "we," "us" and "our" will be deemed to refer to Sio Gene Therapies Inc., Axovant Gene Therapies Ltd. or Axovant Sciences, Inc., as the context requires.

Pavan Cheruvu, M.D., David Nassif, J.D. and Gavin Corcoran, M.D.

Under each of Dr. Cheruvu's, Mr. Nassif's and Dr. Corcoran's employment agreements, such executive officer is eligible for the following severance and change in control benefits, conditioned upon delivering a release of claims in our favor:

- If we terminate the officer's employment without cause or the officer resigns for good reason, in either case, prior to a change in control or more than 12 months following a change in control, then we will pay to the officer a one-time cash payment equal to the sum of his annual base salary, the pro-rated amount of the his annual target bonus in respect of the fiscal year in which the termination of employment occurs, and any unpaid annual bonus amount with respect to the fiscal year ended prior to the termination of his employment. We will also reimburse the officer for continued medical coverage for one year if he timely elects such continued coverage.

- If we terminate the officer's employment without cause or the officer resigns for good reason, in either case, upon or on or before the twelve-month anniversary of a change in control, but not before a change in control, then we will pay to Mr. Nassif or Dr. Corcoran a one-time cash payment equal to 1.5 times, and to Dr. Cheruvu a one-time cash payment equal to two times, the sum of his annual base salary, the pro-rated amount of the his annual target bonus in respect of the fiscal year in which the termination of employment occurs, and any unpaid annual bonus amount with respect to the fiscal year ended prior to the termination of his employment. We will also reimburse the officer for continued medical coverage for 18 months if he timely elects such continued coverage.

- If the officer is subjected to excise tax pursuant to Sections 280G and 4999 of the Internal Revenue Code, he will either have his payments cut back so that the excise tax does not apply, or he will receive the full payments and benefits and be subject to the excise tax, whichever puts him in a better after-tax position.

The definitions of "cause," "good reason" and "change in control" are set forth in the individual employment agreements.

Further, under the terms of our Amended and Restated 2015 Equity Incentive Plan, if Dr. Cheruvu, Mr. Nassif or Dr. Corcoran are employed by us immediately prior to a change in control, then all remaining shares of common stock underlying the officer's outstanding options will vest.

We consider the severance and change in control benefits described above to be critical to attracting and retaining high caliber executives. We believe that appropriately structured severance and change in control benefits, including accelerated vesting provisions, minimize the distractions and reduce the risk that an executive voluntarily terminates his employment with us during times of uncertainty, such as before an acquisition is completed. We believe that our existing arrangements allow each named executive officer to focus on continuing normal business operations and, in the event of a change in control, on the success of a potential business combination, rather than on how business decisions that may be in the best interest of our shareholders will impact his own financial security.

2015 Equity Incentive Plan

In March 2015, our board of directors and our sole shareholder adopted our 2015 Equity Incentive Plan, or the 2015 Plan. In May 2015, our board of directors amended the 2015 Plan and our sole shareholder ratified such amendments. The description of the 2015 Plan set forth below, reflects the 2015 Plan, as amended. Our 2015 Plan provides for the grant of incentive options within the meaning of Section 422 of the Internal Revenue Code, or the Code, to our employees and our subsidiary corporations' employees, and for the grant of nonstatutory options, restricted stock awards, restricted stock unit awards, stock appreciation rights, performance stock awards and other forms of stock compensation to our employees, including officers, consultants and directors. The 2015 Plan also provides for the grant of performance cash awards to our employees, consultants and directors.

Shares issued under the 2015 Plan may be authorized but unissued or reacquired shares of common stock. Shares subject to stock awards granted under the 2015 Plan that expire or terminate without being exercised in full, or that are paid out in cash rather than in shares, will not reduce the number of shares available for issuance under the 2015 Plan. Additionally, shares issued pursuant to stock awards under the 2015 Plan that we repurchase or that are forfeited, as well as shares reacquired by us as consideration for the exercise or purchase price of a stock award or to satisfy tax withholding obligations related to a stock award, will become available for future grant under the 2015 Plan.

Our board of directors, or a duly authorized committee thereof, will have the authority to administer the 2015 Plan. Our board of directors will delegate its authority to administer the 2015 Plan to our compensation committee under the terms of the compensation committee's charter. Our board of directors may also delegate to one or more of our officers the authority to (i) designate employees other than officers to receive specified stock awards and (ii) determine the number of our shares of common stock to be subject to such stock awards. Subject to the terms of the 2015 Plan, the administrator has the authority to determine the terms of awards, including recipients, the exercise price or strike price of stock awards, if any, the number of shares subject to each stock award, the fair market value of a share of common stock, the vesting schedule applicable to the awards, together with any vesting acceleration, the form of consideration, if any, payable upon exercise or settlement of the stock award and the terms and conditions of the award agreements for use under the 2015 Plan.

The administrator has the power to modify outstanding awards under our 2015 Plan. Subject to the terms of the 2015 Plan, the administrator has the authority to reprice any outstanding option or stock appreciation right, cancel and re-grant any outstanding option or stock appreciation right in exchange for new stock awards, cash or other consideration, or take any other action that is treated as a repricing under generally accepted accounting principles, with the consent of any adversely affected participant.

The administrator may provide, in an individual award agreement or in any other written agreement between us and the participant, that the stock award will be subject to additional acceleration of vesting and exercisability in the event of a change in control. In the absence of such a provision, no such acceleration of the stock award will occur.

Our board has the authority to amend, suspend, or terminate the 2015 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. No incentive options may be granted after the tenth anniversary of the date our board of directors adopted the 2015 Plan.

Director Compensation

Non-Employee Director Compensation Policy

Non-employee directors are compensated for service on the Board and its committees through a combination of cash retainers and equity grants. We also reimburse directors for expenses incurred in serving as a director. Directors who are also employed by us are not separately compensated for their service on the Board. Additionally, Dr. Venker does not receive a cash retainer or equity grants.

For our fiscal year ended March 31, 2021, each non-employee director (other than Mr. Oren and Dr. Venker) was paid the following annual amounts quarterly in arrears:

- Board retainer of $40,000
- Audit committee retainer of $9,000 ($20,000 for the Chairperson)
- Compensation Committee retainer of $6,000 ($12,000 for the Chairperson)
- Nominating and Corporate Governance Committee retainer of $5,000 ($8,000 for the Chairperson)

The chairman of the Board receives an annual retainer of $30,000, and the lead independent director receives an annual retainer of $20,000. For the fiscal year ending March 31, 2022, we anticipate that each new non-employee director will receive an initial option grant to purchase 84,000 shares of common stock. In addition, on an annual basis, typically in April, each continuing non-employee director will receive an additional option grant. Option grants have an exercise price equal to the closing price of our common stock on Nasdaq on the grant date. Initial grants vest in three equal annual installments, and annual grants vest in full on the first anniversary of the grant date, in each case subject to the non-employee director's continuous service through the vesting date. Option grants to non-employee directors expire on the ten-year anniversary of the grant date. In April 2019, the Compensation Committee adopted a policy that all directors serving as of an annual grant date shall be eligible for equity awards regardless of the date of their appointment to the Board.

Director Compensation for Fiscal Year Ended March 31, 2021

The following table shows, for our fiscal year ended March 31, 2021, certain information with respect to the compensation of our non-employee directors:

Name	Fee Earned or Paid in Cash	Option Awards[1]	Total
Current Directors			
Frank Torti, M.D.	$ 75,500	$ 49,254 [2]	$ 124,754
Atul Pande, M.D.	83,000	49,254 [2]	132,254
Berndt Modig	61,000	49,254 [2]	110,254
Senthil Sundaram	64,694	49,254 [2]	113,948
Eric Venker, M.D., Pharm.D. [3]	—	—	—
Kristiina Vuori, M.D., Ph.D. [4]	22,011	162,556 [5]	184,567
Former Directors			
Ilan Oren [6]	—	—	—

[1] Amounts reported in this column do not reflect the amounts actually received by the director. Instead, these amounts reflect the aggregate grant date fair value of each stock option and the incremental fair value related to the accelerated vesting of stock options granted to certain directors during the fiscal year, as computed in accordance with FASB ASC 718.

[2] In April 2020, each of Dr. Torti, Dr. Pande, Mr. Modig and Mr. Sundaram was granted an option to purchase 17,500 shares of common stock with an exercise price of $3.45 per share. The shares subject to the options will vest on the first anniversary of the date of the grant.

[3] Dr. Venker was appointed to our Board in February 2019 and has declined to receive any cash or equity compensation for his service as a director.

[4] Dr. Vuori was appointed to our Board in October 2020.

[5] In October 2020, Dr. Vuori was granted an option to purchase 35,000 shares of common stock with an exercise price of $5.63 per share. The shares subject to the options will vest in three equal installments on the annual anniversary of the date of appointment.

[6] Mr. Oren, since his re-appointment to the Board in June 2018, has declined to receive any cash or equity compensation for his service as a director. Mr. Oren was not nominated to stand for re-election at our annual meeting of shareholders for 2020. Effective September 24, 2020, the date of such meeting, Mr. Oren is no longer a member of our Board.

The following table provides information regarding the aggregate number of stock options held by each of our non-employee directors as of March 31, 2021, as adjusted to reflect a 1-for-8 reverse stock split effected in May 2019:

Name	Outstanding Stock Options [1]
Current Directors	
Frank Torti, M.D.	68,125
Atul Pande, M.D.	77,375
Berndt Modig	68,885
Senthil Sundaram	36,250
Kristiina Vuori, M.D., Ph.D.	35,000

[1] All of these options allow for early exercise, subject to our repurchase option with respect to any unvested shares of common stock. In addition, all shares of common stock underlying options held by our directors will become fully vested upon a change in control, as that term is defined in our Amended and Restated 2015 Equity Incentive Plan.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters

The following table sets forth certain information regarding the ownership of our shares of common stock as of April 30, 2021, by:

- all those known by us to be beneficial owners of more than five percent of our shares of common stock;
- each of the executive officers named in the Summary Compensation Table;
- each of our directors; and
- all of our executive officers and directors of as a group.

This table is based upon information supplied by officers, directors and principal shareholders and filings with the SEC. Unless otherwise indicated in the footnotes to this table and subject to community property laws where applicable, we believe that each of the shareholders named in this table has sole voting and dispositive power with respect to the shares indicated as beneficially owned. We have deemed shares of common stock subject to options that are currently exercisable or exercisable within 60 days of April 30, 2021, to be outstanding and to be beneficially owned by the person holding the option for the purpose of computing the percentage ownership of that person but have not treated them as outstanding for the purpose of computing the percentage ownership of any other person.

Applicable percentages are based on 69,558,434 shares outstanding on April 30, 2021, adjusted as required by rules promulgated by the SEC. Except as set forth below, the principal business address of each such person or entity is c/o Sio Gene Therapies Inc., 130 West 42nd Street, 26th Floor, New York, New York 10036. All figures reflect a 1-for-8 reverse stock split effected in May 2019.

Beneficial Owner	Number of Shares Beneficially Owned	Percent of Shares Beneficially Owned
5% Shareholder:		
Roivant Sciences Ltd. [1]	18,577,380	26.71%
Consonance Capital Management LP [2]	6,488,333	8.91
Suvretta Capital Management, LLC[3]	5,489,000	7.89
Named Executive Officers and Directors:		
Pavan Cheruvu. M.D. [4]	1,723,216	2.42
David Nassif, J.D. [5]	594,438	*
Gavin Corcoran, M.D. [6]	525,051	*
Atul Pande, M.D. [7]	152,745	*
Berndt Modig [8]	120,624	*
Frank Torti, M.D. [9]	110,125	*
Senthil Sundaram [10]	78,250	*
Kristiina Vuori, M.D., Ph.D. [11]	77,000	*
Eric Venker, M.D., Pharm.D.	—	—
All executive officers and directors as a group (9 persons)	3,381,449	4.65%

* Represents beneficial ownership of less than one percent

[1] As reported on a Schedule 13D/A filed by RSL on February 28, 2020, RSL directly owns and has sole voting power over 18,577,380 shares of common stock. Sakshi Chhabra, Andrew Lo, Patrick Machado, Keith Manchester, M.D., Daniel Gold, Ilan Oren, Masayo Tada and Vivek Ramaswamy are the members of the board of directors of RSL and may be deemed to have shared voting, investment and dispositive power with respect to the shares held by this entity. These individuals disclaim beneficial ownership with respect to such shares except to the extent of their pecuniary interest therein. The principal business address of RSL is c/o Roivant Sciences Ltd., Suite 1, 3rd Floor, 11-12 St. James's Square, London, SW1Y 4LB, United Kingdom.

[2] As reported on a Schedule 13F-HR filed by Consonance Capital Management LP on May 17, 2021, Consonance Capital Management LP directly owns and has sole voting power over 3,186,335 shares of common stock. Consonance Capital Management LP also owns pre-funded warrants to purchase up to 3,301,998 shares of common stock with an exercise price of $0.00001 per share, which are immediately exercisable and are included in the number of shares of common stock beneficially owned in the table above. The address of Consonance Capital Management LP is 1370 Avenue of the Americas Suite 3301 New York NY 10019.

[3] As reported on a Schedule 13F-HR filed by Suvretta Capital Management, LLC on May 17, 2021. Suvretta Capital Management, LLC holds 5,489,000 shares of common stock. The address of Suvretta Capital Management, LLC is 540 Madison Avenue, 7th Floor, New York NY 10022.

[4] Represents (i) 180,426 shares of common stock; (ii) 37,567 vested restricted stock units and (iii) 1,505,223 shares of common stock issuable pursuant to immediately exercisable options, including 1,153,,645 shares issuable following exercise of such options that remain unvested within 60 days after April 30, 2021.

[5] Represents (i) 34,004 shares of common stock; (ii) 17,534 vested restricted stock units and (iii) 542,900 shares of common stock issuable pursuant to immediately exercisable options, including 457,550 shares issuable following exercise of such options that remain unvested within 60 days after April 30, 2021.

[6] Represents (i) 25,792 shares of common stock; (ii)14,134 vested restricted stock units and (iii) 485,125 shares of common stock issuable pursuant to immediately exercisable options, including 399,768 shares issuable following exercise of such options that remain unvested within 60 days after April 30, 2021.

[7] Represents (i) 33,370 shares of common stock and (ii) 119,375 shares of common stock issuable pursuant to immediately exercisable options, including 42,000 shares issuable following exercise of such options that remain unvested within 60 days after April 30, 2021.

[8] Represents (i) 9,739 shares of common stock and (ii) 110,885 shares of common stock issuable pursuant to immediately exercisable options, including 42,000 shares issuable following exercise of such options that remain unvested within 60 days after April 30, 2021.

[9] Represents 110,125 shares of common stock issuable pursuant to immediately exercisable options, including 48,250 shares issuable following exercise of such options that remain unvested within 60 days after April 30, 2021.

[10] Represents 78,250 shares of common stock issuable pursuant to immediately exercisable options, including 48,250 shares issuable following exercise of such options that remain unvested within 60 days after April 30, 2021.

[11] Represents 77,000 shares of common stock issuable pursuant to immediately exercisable options, including 77,000 shares issuable following exercise of such options that remain unvested within 60 days after April 30, 2021.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our directors and executive officers, and persons who own more than ten percent of a registered class of our equity securities, to file with the SEC initial reports of ownership and reports of changes in ownership of shares of common stock and other equity securities of Sio. Officers, directors and greater than ten percent shareholders are required by SEC regulation to furnish us with copies of all Section 16(a) forms they file.

To our knowledge, based solely on a review of the copies of such reports furnished to us and written representations that no other reports were required, during our fiscal years ended March 31, 2021 and March 31, 2020, all Section 16(a) filing requirements applicable to our officers, directors and greater than ten percent beneficial owners were complied with, except as follows. Roivant Sciences Ltd. acquired an additional 5,333,333 shares of our common stock in an underwritten public offering we conducted that closed on February 24, 2020. Due to an administrative error, Roivant Sciences Ltd. reported this transaction on a Form 4 filed with the SEC on February 27, 2020.

Equity Compensation Plan Information

The following table shows information regarding our equity compensation plan as of March 31, 2021:

Plan Category	Number of shares of common stock to be issued upon exercise of outstanding options and rights (a)		Weighted-average exercise price of outstanding options and rights (b)	Number of shares of common stock available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)	
Equity compensation plans approved by shareholders	3,121,759	(1)	$ 12.26	2,031,392	(2)
Equity compensation plans not approved by shareholders	—		—	—	
Total	3,121,759		$ 12.26	2,031,392	

(1) Includes RSUs representing 1,026,216 shares of our common stock, which have no exercise price.

(1) Pursuant to the terms of our Amended and Restated 2015 Equity Incentive Plan, an additional 2,775,102 shares were added to the number of available shares effective April 1, 2021.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Transactions With Related Persons

Related-Person Transactions Policy and Procedures

We have adopted a written Related-Person Transactions Policy that sets forth our policies and procedures regarding the identification, review, consideration and approval or ratification of "related-person transactions." For purposes of our policy only, a "related-person transaction" is a transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which we and any "related person" are participants involving an amount that exceeds $120,000. Transactions involving compensation for services provided to us as an employee, director, consultant or similar capacity by a related person are not covered by this policy. A related person is any executive officer, director, or more than 5% shareholder of Sio Gene Therapies Inc., including any of their immediate family members, and any entity owned or controlled by such persons.

Under the policy, where a transaction has been identified as a related-person transaction, management must present information regarding the proposed related-person transaction to the Audit Committee (or, where Audit Committee approval would be inappropriate, to another independent body of the Board) for consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction and whether any alternative transactions were available. To identify related-person transactions in advance, we rely on information supplied by our executive officers, directors and certain significant shareholders. In considering related-person transactions, the Audit Committee takes into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us;
- the impact on a director's independence in the event the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the terms of the transaction;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from employees generally. In the event a director has an interest in the proposed transaction, the director must recuse himself or herself from the deliberations and approval.

The policy requires that, in determining whether to approve, ratify or reject a related-person transaction, the Audit Committee considers, in light of known circumstances, whether the transaction is in, or is not inconsistent with, the best interests of Sio and its shareholders, as the Audit Committee determines in the good faith exercise of its discretion.

Related-Person Transactions

The following is a description of transactions since April 1, 2019, or any currently proposed transaction, in which we were or are to be a participant and the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or holders of more than 5% of our share capital, or any members of their immediate family, had or will have a direct or indirect material interest. The share and per share amounts set forth in this section have been adjusted for our 1-for-8 reverse stock split effected in May 2019.

RSL Financing Participation

In February 2020, we issued and sold 16,631,336 shares of common stock and pre-funded warrants to purchase up to 3,301,998 shares of common stock in a follow-on public offering, including 2,600,000 shares of common stock sold pursuant to the exercise of the underwriters' option to purchase additional shares and also including 5,333,333 shares of common stock issued and sold to RSL, at an offering price of $3.75 per share of common stock and $3.74999 per pre-funded warrant.

Information Sharing and Cooperation Agreement

In June 2018, we entered into an amended and restated information sharing and cooperation agreement with RSL (the Cooperation Agreement"), which became effective concurrently with the closing of the private placement to RSL in July 2018. The Cooperation Agreement, among other things:

- obligates us to deliver to RSL periodic financial statements and other information upon reasonable request and to comply with other specified financial reporting requirements;
- requires us to supply certain material information to RSL to assist it in preparing any future SEC filings; and
- requires us to implement and observe certain policies and procedures related to applicable laws and regulations.

We have agreed to indemnify RSL and its affiliates and their respective officers, employees and directors against all losses arising out of, due to or in connection with RSL's status as a shareholder under the Cooperation Agreement and the operations of or services provided by RSL or its affiliates or their respective officers, employees or directors to us or any of our subsidiaries, subject to certain limitations set forth in the Cooperation Agreement.

Subject to specified exceptions, the Cooperation Agreement will terminate at such time as RSL is no longer required (a) under Generally Accepted Accounting Principles in the United States, or U.S. GAAP, to consolidate our results of operations and financial position, (b) under U.S. GAAP to account for its investment in us under the equity method of accounting, or (c) otherwise to include our separate financial statements in its filings with the SEC pursuant to any SEC rule. In addition, the Cooperation Agreement may be terminated upon mutual written consent of the parties or upon written notice from RSL to us in the event of our bankruptcy, liquidation, dissolution or winding-up.

Affiliate Services Agreements

We have entered into services agreements with RSI and Roivant Sciences GmbH (collectively, the "Service Providers"), each a wholly owned subsidiary of RSL, pursuant to which the Service Providers provide us with services in relation to the identification of potential product candidates and project management of clinical trials, as well as other services related to our development, administrative and financial functions (the "Services Agreements"). Under the terms of the Services Agreements, we are obligated to pay or reimburse the Service Providers for the costs they, or third parties acting on their behalf, incur in providing services to us, including administrative and support services as well as research and development services. In addition, we are obligated to pay to the Service Providers at a predetermined mark-up on any general and administrative and research and development services incurred directly by the Service Providers. For the years ended March 31, 2021 and 2020, we incurred expenses of $0.1 million and $0.1 million, respectively, under the Services Agreements, inclusive of the mark-up, which have been treated as capital contributions. Going forward, the costs allocated to us under the Services Agreements with the Service Providers are expected to continue to be insignificant.

Indemnification Agreements

We have entered into indemnity agreements with our officers and directors which provide, among other things, that we will indemnify such officer or director, under the circumstances and to the extent provided for therein, for expenses, damages, judgments, fines and settlements he or she may be required to pay in actions or proceedings which he or she is or may be made a party by reason of his or her position as a director, officer or other agent of ours.

Independence of the Board of Directors

After review of all relevant identified transactions or relationships between each director, or any of his family members, and Sio, our senior management and our independent auditors, the Board has affirmatively determined that the following four individuals are independent directors within the meaning of the applicable SEC and Nasdaq listing rules: Mr. Modig, Dr. Pande, Mr. Sundaram and Dr. Vuori. In making this determination, the Board found that none of these directors had a material or other disqualifying relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. The Board has determined that Dr. Cheruvu, by virtue of his position as our principal executive officer, and Dr. Torti and Dr. Venker, by virtue of their positions with RSI, are not independent under applicable SEC and Nasdaq listing rules.

Item 14. Principal Accounting Fees and Services

Independent Registered Public Accounting Firm Fees and Services

The following table presents aggregate fees billed by Ernst & Young LLP for our fiscal years ended March 31, 2021 and 2020:

	Fiscal Year Ended March 31, 2021	Fiscal Year Ended March 31, 2020
Audit Fees[1]	$ 752,062	$ 597,275
Audit Related Fees	—	—
Tax Fees[2]	—	—
All Other Fees	—	2,000
Total Fees	$ 752,062	$ 599,275

[1] Includes fees for the audit of our annual consolidated financial statements, included in our Annual Report on Form 10-K, review of the unaudited consolidated financial statements included in our Quarterly Reports on Form 10-Q, and for services that are normally provided by Ernst & Young LLP in connection with statutory and regulatory filings or engagements, including issuance of consents.

[2] Includes fees for professional services for international tax compliance, supporting other tax-related regulatory requirements primarily in the transfer pricing area, and international tax consulting and planning services.

All of the fees described above were pre-approved by the Audit Committee.

Pre-Approval Policies and Procedures

The Audit Committee has adopted a policy and procedures for the pre-approval of audit and non-audit services rendered by our independent registered public accounting firm. The policy generally pre-approves specified services in the defined categories of audit services, audit-related services and tax services up to specified amounts. Pre-approval may also be given as part of the Audit Committee's approval of the scope of the engagement of the independent registered public accounting firm or on an individual, explicit, case-by-case basis before the independent registered public accounting firm is engaged to provide each service. The pre-approval of services may be delegated to one or more of the Audit Committee's members, but the decision must be reported to the full Audit Committee at its next scheduled meeting.

PART IV. FINANCIAL INFORMATION

Item 15. Exhibits and Financial Statements Schedules

(a) Documents filed as part of this Annual Report on Form 10-K:

(1) Financial Statements. The Consolidated Financial Statements are included as Appendix A hereto and are filed as part of this Annual Report on Form 10-K. The Consolidated Financial Statements include:

(2) Exhibits. The exhibits set forth below on the Exhibit Index to this annual report are filed as part of this Annual Report on Form 10-K. This list of exhibits identifies each management contract or compensatory plan or arrangement required to be filed as an exhibit to this Annual Report on Form 10-K.

Exhibit Index

Exhibit No.	Description of Document	Schedule/Form	File No.	Exhibit No.	Filing Date
3.1	Certificate of Incorporation.	8-K12G3	000-56226	3.1	11/13/2020
3.2	Bylaws.	8-K12G3	000-56226	3.2	11/13/2020
4.1	Form of Common Stock Certificate.	8-K12G3	000-56226	4.1	11/13/2020
4.2†	Description of Securities.				
4.3†	Form of Pre-funded Warrant to purchase Shares of Common Stock.				
10.1	Waiver and Option Agreement, dated as of May 8, 2015, by and between Roivant Sciences Ltd. and the Registrant.	S-1/A	333-204073	10.9	05/22/2015
10.2+	Form of Indemnification Agreement with directors and executive officers.	S-1/A	333-204073	10.4	05/22/2015
10.3+	Non-Employee Director Compensation Policy.	10-K	001-37418	10.12	06/13/2017
10.4	Amended and Restated Information Sharing and Cooperation Agreement, dated as of June 5, 2018, by and between the Registrant and Roivant Sciences Ltd.	10-Q	001-37418	10.1	08/07/2018
10.5*	License Agreement, dated as of June 5, 2018, by and between the Registrant and Oxford Biomedica (UK) Ltd.	10-Q	001-37418	10.3	08/07/2018
10.6*	Exclusive License Agreement, dated as of December 7, 2018, by and between the Registrant and the University of Massachusetts.	10-Q	001-37418	10.1	02/07/2019
10.7	Amended and Restated Services Agreement, effective as of June 10, 2019, by and among Roivant Sciences, Inc. and the Registrant.	10-K	001-37418	10.21	06/11/2019
10.8	Amended and Restated Services Agreement, effective as of June 10, 2019, by and among Roivant Sciences GmbH and the Registrant.	10-K	001-37418	10.22	06/11/2019
10.9+	Employment Agreement, dated November 4, 2019, by and between Pavan Cheruvu and the Registrant.	8-K	001-37418	10.1	11/08/2019

Exhibit No.	Description of Document	Schedule/Form	File No.	Exhibit No.	Filing Date
10.10+	Employment Agreement, dated November 4, 2019, by and between David Nassif and the Registrant.	8-K	001-37418	10.2	11/08/2019
10.11+	Employment Agreement, dated November 4, 2019, by and between Gavin Corcoran and the Registrant.	8-K	001-37418	10.3	11/08/2019
10.12+	Amended and Restated 2015 Equity Incentive Plan.	S-8 POS	333-244371	10.1	11/13/2020
10.13+	Forms of Option Grant Notice and Option Agreement under the Amended and Restated 2015 Equity Incentive Plan.	S-8 POS	333-244371	10.2	11/13/2020
10.14+	Form of Early Exercise Stock Purchase Agreement under the Amended and Restated 2015 Equity Incentive Plan.	S-8 POS	333-244371	10.3	11/13/2020
10.15	Sales Agreement, dated as of December 16, 2020, between the Registrant and SVB Leerink LLC.	8-K	001-37418	1.1	12/18/2020
10.16†+	Forms of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under the Amended and Restated 2015 Equity Incentive Plan.				
21.1†	Subsidiaries of the Registrant.				
23.1†	Consent of Ernst & Young LLP, independent registered public accounting firm.				
24.1†	Power of Attorney (included on signature page).				
31.1†	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2†	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1†**	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
32.2†**	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.INS XBRL	Instance Document				
101.SCH XBRL	Taxonomy Extension Schema				
101.CAL XBRL	Taxonomy Extension Calculation Linkbase				
101.DEF XBRL	Taxonomy Extension Definition Linkbase				
101.LAB XBRL	Taxonomy Extension Label Linkbase				
101.PRE XBRL	Taxonomy Extension Presentation Linkbase				

† Filed herewith.

+ Indicates management contract or compensatory plan.

* Confidential treatment has been granted for portions omitted from this exhibit (indicated by asterisks) and those portions have been separately filed with the Securities and Exchange Commission.

** In accordance with Item 601(b)(32)(ii) of Regulation S-K and SEC Release Nos. 33-8238 and 34-47986, Final Rule: Management's Reports on Internal Control Over Financial Reporting and Certification of Disclosure in Exchange Act Periodic Reports, these certifications are being furnished solely to accompany this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of 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.

SIO GENE THERAPIES INC.

June 9, 2021

By: /s/ Pavan Cheruvu
Pavan Cheruvu
Chief Executive Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Pavan Cheruvu and David Nassif, jointly and severally, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his name, place and stead, in any and all capacities, to sign this Annual Report on Form 10-K of Sio Gene Therapies Inc., and any or all amendments thereto, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Pavan Cheruvu Pavan Cheruvu	Chief Executive Officer and Director (Principal Executive Officer)	June 9, 2021
/s/ David Nassif David Nassif	Chief Financial Officer and Chief Accounting Officer, General Counsel (Principal Financial Officer and Principal Accounting Officer)	June 9, 2021
/s/ Frank Torti Frank Torti	Director, Chairman of the Board	June 9, 2021
/s/ Atul Pande Atul Pande	Director, Lead Independent Director	June 9, 2021
/s/ Berndt Modig Berndt Modig	Director	June 9, 2021
/s/ Senthil Sundaram Senthil Sundaram	Director	June 9, 2021
/s/ Eric Venker Eric Venker	Director	June 9, 2021
/s/ Kristiina Vuori Kristiina Vuori	Director	June 9, 2021

INDEX TO THE CONSOLIDATED FINANCIAL STATEMENTS OF SIO GENE THERAPIES INC.

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Sio Gene Therapies Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Sio Gene Therapies Inc. (the Company) as of March 31, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, shareholders' equity and cash flows for each of the two years in the period ended March 31, 2021, 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 March 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended March 31, 2021, 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 disclosure to which it relates.

Clinical Study Accrual

Description of the Matter	As discussed in Note 2 to the consolidated financial statements, the estimated costs of research and development activities conducted by third-party service providers, which primarily include activities associated with clinical studies, are accrued over the service periods specified in the contracts and adjusted as necessary based upon an ongoing review of the level of effort and costs actually incurred. Auditing the Company's accrual for clinical study costs was complex because information necessary to estimate the accrual is accumulated from third parties, and the Company's assessment of the completeness of the information is subject to variability and uncertainty. In addition, in certain circumstances, the determination of the nature and amount of services that have been received during the reporting period requires judgment as the timing and pattern of vendor invoicing does not correspond to the level of services provided.
How We Addressed the Matter in Our Audit	To test the clinical study accrual, our audit procedures included, among others, reading a sample of the Company's agreements with the service providers, including pending amendments, to understand key financial and contractual terms, assessing the impact of these terms on the accrual and testing the accuracy and completeness of the underlying data used in the accrual computations. We also evaluated management's estimates of the vendors' progress for a sample of clinical studies by making direct inquiries of the Company's operations personnel overseeing the clinical studies and obtaining information about the service providers' estimate of costs that had been incurred through March 31, 2021. To evaluate the completeness and valuation of the accrual, we also inspected subsequent invoices received from the service providers and cash disbursements to the service providers, to the extent such invoices were received, or payments were made prior to the date that the consolidated financial statements were issued.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2016.

Iselin, New Jersey

June 9, 2021

SIO GENE THERAPIES INC.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	March 31, 2021	March 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 118,986	$ 80,752
Receivable from sale of long-term investment	4,343	—
Prepaid expenses and other current assets	7,348	2,971
Income tax receivable	1,656	1,707
Total current assets	132,333	85,430
Long-term investment	—	5,871
Other non-current assets	—	46
Long-term restricted cash	1,184	—
Operating lease right-of-use assets	1,152	1,532
Property and equipment, net	478	801
Total assets	$ 135,147	$ 93,680
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 1,341	$ 4,412
Accrued expenses	9,196	11,319
Current portion of operating lease liabilities	311	889
Current portion of long-term debt	—	15,423
Total current liabilities	10,848	32,043
Operating lease liabilities, net of current portion	932	79
Total liabilities	11,780	32,122
Commitments and contingencies (Note 12)		
Shareholders' equity:		
Common stock, par value $0.00001 per share, 1,000,000,000 shares authorized, 69,377,567 and 39,526,299 issued and outstanding at March 31, 2021 and March 31, 2020, respectively	1	—
Accumulated other comprehensive income (loss)	335	(55)
Additional paid-in capital	914,100	820,257
Accumulated deficit	(791,069)	(758,644)
Total shareholders' equity	123,367	61,558
Total liabilities and shareholders' equity	$ 135,147	$ 93,680

The accompanying notes are an integral part of these consolidated financial statements.

SIO GENE THERAPIES INC.
Consolidated Statements of Operations
(in thousands, except share and per share amounts)

	Years Ended March 31,	
	2021	**2020**
Operating expenses:		
Research and development expenses		
(includes $1,583 and $2,772 of stock-based compensation expense for the years ended March 31, 2021 and 2020, respectively)	$ 24,903	$ 47,110
General and administrative expenses		
(includes $2,909 and $5,123 of stock-based compensation expense for the years ended March 31, 2021 and 2020, respectively)	17,294	22,061
Total operating expenses	42,197	69,171
Interest expense	799	4,377
Other income	(10,359)	(1,358)
Loss before income tax (benefit) expense	(32,637)	(72,190)
Income tax (benefit) expense	(212)	438
Net loss	$ (32,425)	$ (72,628)
Net loss per share of common stock — basic and diluted	$ (0.62)	$ (2.93)
Weighted average shares of common stock outstanding — basic and diluted	52,181,398	24,812,536

The accompanying notes are an integral part of these consolidated financial statements.

SIO GENE THERAPIES INC.
Consolidated Statements of Comprehensive Loss
(in thousands)

	Years Ended March 31,	
	2021	**2020**
Net loss	$ (32,425)	$ (72,628)
Other comprehensive income (loss):		
Foreign currency translation adjustment	390	(966)
Total other comprehensive income (loss)	390	(966)
Comprehensive loss	$ (32,035)	$ (73,594)

The accompanying notes are an integral part of these consolidated financial statements.

SIO GENE THERAPIES INC.
Consolidated Statements of Shareholders' Equity
(in thousands, except share and per share amounts)

	Common Stock		Additional Paid -in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Shareholders' Equity
	Shares	Amount				
Balance at March 31, 2019	22,779,891	$ —	$ 741,318	$ (686,016)	$ 911	$ 56,213
Issuance of shares upon exercise of stock options	11,778	—	86	—	—	86
Shares issued upon settlement of restricted stock units	103,294	—	—	—	—	—
Shares and pre-funded warrants sold in public offering, net of underwriting discounts and commissions and offering expenses of $3.9 million	16,631,336	—	70,810	—	—	70,810
Stock-based compensation expense	—	—	7,895	—	—	7,895
Capital contribution received from Roivant Sciences, Inc.	—	—	148	—	—	148
Foreign currency translation adjustment	—	—	—	—	(966)	(966)
Net loss	—	—	—	(72,628)	—	(72,628)
Balance at March 31, 2020	39,526,299	$ —	$ 820,257	$ (758,644)	$ (55)	$ 61,558
Shares issued upon settlement of restricted stock units	187,741	—	—	—	—	—
Shares sold in connection with at-the-market offering, net of brokerage fees and offering expenses of $4.0 million	29,663,527	1	89,230	—	—	89,231
Stock-based compensation expense	—	—	4,492	—	—	4,492
Capital contribution received from Roivant Sciences, Inc.	—	—	121	—	—	121
Foreign currency translation adjustment	—	—	—	—	390	390
Net loss	—	—	—	(32,425)	—	(32,425)
Balance at March 31, 2021	69,377,567	$ 1	$ 914,100	$ (791,069)	$ 335	$ 123,367

The accompanying notes are an integral part of these consolidated financial statements.

SIO GENE THERAPIES INC.
Consolidated Statements of Cash Flows
(in thousands)

	Years Ended March 31,	
	2021	**2020**
Cash flows from operating activities:		
Net loss	$ (32,425)	$ (72,628)
Adjustments to reconcile net loss to net cash used in operating activities:		
Unrealized foreign currency translation adjustment	390	(966)
Amortization of operating lease right-of-use assets	1,521	1,617
Stock-based compensation expense	4,492	7,895
Depreciation and non-cash amortization	945	1,477
Gains on long-term investment	(11,256)	—
Change in operating lease liabilities	(866)	(1,582)
Other	84	19
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(4,377)	2,892
Income tax receivable	51	19
Other non-current assets	46	340
Accounts payable	(3,071)	2,710
Accrued expenses	(2,123)	(9,266)
Net cash used in operating activities	(46,589)	(67,473)
Cash flows from investing activities:		
Cash proceeds from sale of long-term investment	12,784	—
Purchases of property and equipment	(398)	(255)
Net cash provided by (used in) investing activities	12,386	(255)
Cash flows from financing activities:		
Payments on long-term debt	(15,731)	(29,563)
Capital contribution received from Roivant Sciences, Inc.	121	148
Cash proceeds from stock option exercises	—	86
Cash proceeds from issuance of shares of common stock and pre-funded warrants, net of issuance costs	89,231	70,810
Net cash provided by financing activities	73,621	41,481
Net change in cash and cash equivalents and long-term restricted cash	39,418	(26,247)
Cash and cash equivalents—beginning of year	80,752	106,999
Total cash and cash equivalents and long-term restricted cash—end of year	$ 120,170	$ 80,752
Cash and cash equivalents—end of year	118,986	80,752
Restricted cash included in long-term assets—end of year	1,184	—
Total cash and cash equivalents and long-term restricted cash—end of year	$ 120,170	$ 80,752
Non-cash operating activities:		
Operating lease right-of-use assets recognized upon and since the adoption of ASC 842, *Leases*, on April 1, 2019	$ 1,141	$ 3,103
Operating lease liabilities recognized upon and since the adoption of ASC 842, *Leases*, on April 1, 2019	1,141	2,517
Amounts reclassified from other non-current assets to operating lease right-of-use assets upon the adoption of ASC 842, *Leases*, on April 1, 2019	—	586
Supplemental disclosure of cash paid:		
Income taxes	$ 40	$ 562
Interest	$ 465	$ 4,012

The accompanying notes are an integral part of these consolidated financial statements.

Note 1—Description of Business

Sio Gene Therapies Inc. ("Sio"), together with its wholly owned subsidiaries (the "Company"), is a clinical-stage company focused on developing gene therapies for neurodegenerative diseases. The Company is developing a pipeline of innovative product candidates for the treatment of these debilitating diseases, including GM1 gangliosidosis, GM2 gangliosidosis (including Tay-Sachs and Sandhoff diseases) and Parkinson's disease. The Company is dedicated to realizing the potential of gene therapies to offer transformative patient outcomes in areas of high unmet medical need.

Sio is a Delaware corporation, which was originally an exempted limited company incorporated under the laws of Bermuda in October 2014 and was named Axovant Gene Therapies Ltd. ("AGT") from March 2019 until November 2020. During November 2020, the Company completed a corporate transformation, changing its jurisdiction of incorporation from Bermuda to the State of Delaware, changing its name to Sio Gene Therapies Inc., and changing its ticker symbol on The Nasdaq Global Select Market (“Nasdaq”) to “SIOX” (collectively, these events comprise the “Domestication”). The Company continues to be subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and applicable rules of Nasdaq.

Since its initial public offering in 2015, the Company has devoted substantially all of its efforts to raising capital, acquiring product candidates and advancing its product candidates into clinical development. The Company has determined that it has one operating and reporting segment as it allocates resources and assesses financial performance on a consolidated basis. The Company does not expect to generate revenue unless and until it successfully completes development and obtains regulatory approval for one of its product candidates.

Note 2—Summary of Significant Accounting Policies

(A) Basis of Presentation:

The Company’s fiscal year ends on March 31, and its fiscal quarters end on June 30, September 30, and December 31.

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and as amended by Accounting Standards Updates ("ASU") issued by the Financial Accounting Standards Board ("FASB"). These consolidated financial statements and accompanying notes include the accounts of the Company and its wholly owned subsidiaries. The Company has no unconsolidated subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. Certain prior period balances have been reclassified to conform to the current period presentation.

During November 2020, the historical financial statements and subsidiaries of AGT became the historical financial statements and subsidiaries of Sio upon consummation of the Domestication. As a result, these consolidated financial statements and accompanying notes reflect (i) the historical operating results of AGT and its subsidiaries prior to the Domestication; (ii) the operating results of the Company following the Domestication; and (iii) the Company’s equity structure for all periods presented.

A 1-for-8 reverse stock split of the Company's outstanding common stock was effected in May 2019 as approved by the Company's Board of Directors and a majority of its shareholders. As such, all references to share and per share amounts in these financial statements and accompanying notes have been retroactively restated to reflect the 1-for-8 reverse stock split, except for the authorized number of shares of the Company's common stock and the par value per share, which were not affected.

(B) Going Concern and Management's Plans:

The Company assesses and determines its ability to continue as a going concern in accordance with the provisions of ASC Subtopic 205-40, "*Presentation of Financial Statements—Going Concern*" ("ASC Subtopic 205-40"), which requires the Company to evaluate whether there are conditions or events that raise substantial doubt about its ability to continue as a going concern within one year after the date that its annual and interim consolidated financial statements are issued. Certain additional financial statement disclosures are required if such conditions or events are identified. If and when an entity’s liquidation becomes imminent, financial statements should be prepared under the liquidation basis of accounting. Determining the extent, if any, to which conditions or events raise substantial doubt about the Company’s ability to continue as a going concern, or the extent to which mitigating plans sufficiently alleviate any such substantial doubt, as well as whether or not liquidation is imminent, requires judgment by management. The Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company’s ability to continue as a going concern within one year after the date the consolidated financial statements are issued.

The Company is currently a development stage company, and thus, has not yet achieved profitability. The Company expects to continue to incur significant operating and net losses, as well as negative cash flows from operations, for the foreseeable future as it continues to develop its gene therapy product candidates and prepares for potential future regulatory approvals and commercialization of its products. The Company has not generated any revenue to date and does not expect to generate product revenue unless and until it successfully completes development and obtains regulatory approval for at least one of its gene therapy product candidates. The Company's current cash and cash equivalents balance will also not be sufficient to complete all necessary development activities and commercially launch its products.

For the years ended March 31, 2021 and March 31, 2020, the Company incurred net losses of $32.4 million and $72.6 million, respectively. As of March 31, 2021, the Company's cash and cash equivalents totaled $119.0 million and its accumulated deficit was $791.1 million. The Company estimates that its significantly increased current cash and cash equivalents balance, which includes cash proceeds received from its sales agreement with SVB Leerink LLC to sell shares of common stock from time to time through an at-the-market equity offering program, as well as cash proceeds received in connection with the sale of its long-term investment in Arvelle Therapeutics B.V. ("Arvelle"), is sufficient to support operations beyond the twelve month period following the date that these consolidated financial statements were issued, including beyond the expected dates of major upcoming milestones for the Company's AXO-AAV-GM1 gene therapy program for the treatment of GM1 gangliosidosis. As such, the Company has determined that there is no longer substantial doubt about its ability to continue as a going concern for the one-year period following the date that these consolidated financial statements and footnotes were issued. These estimates are based on assumptions that may prove to be wrong, and the Company could use its available capital resources sooner than it currently expects.

In order to meet the Company's long-term operating requirements, the Company will need, among other things, additional capital resources. The Company continually assesses multiple options to obtain additional funding to support its operations, including proceeds from offerings of its equity securities or debt, or transactions involving product development, technology licensing or collaboration arrangements, or other sources of capital to complete its currently planned development programs. Management can provide no assurances that it can raise a sufficient amount of financing for the Company on favorable terms, if at all.

(C) Use of Estimates:

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. The Company regularly evaluates estimates and assumptions related to certain assets and liabilities, including its research and development accruals, as well as assumptions used to estimate the fair value of its stock option awards, estimate its income tax expense and estimate its ability to continue as a going concern. Specifically, the Company’s assessment of the completeness of the information for research and development accruals is subject to variability and uncertainty. In addition, in certain circumstances, the determination of the nature and amount of research and development services that have been received during the reporting period requires judgment as the timing and pattern of vendor invoicing does not correspond to the level of services provided. The Company estimates the grant date fair value of stock option awards with only time-based vesting requirements using a Black-Scholes valuation model and uses a Monte Carlo Simulation method under the income approach to estimate the grant date fair value of stock option awards with market-based performance conditions. The Company bases its estimates and assumptions on historical experience and on various other factors that it believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ from those estimates.

Additionally, the Company assessed the impact that the COVID-19 pandemic has had on its operations and financial results as of March 31, 2021 and through the date of issuance of these audited consolidated financial statements. The Company’s analysis was informed by the facts and circumstances as they were known to the Company. This assessment considered the impact COVID-19 may have on financial estimates and assumptions that affect the reported amounts of assets and liabilities and expenses.

(D) Risks and Uncertainties:

The Company is subject to risks common to companies in the pharmaceutical industry including, but not limited to, uncertainties related to commercialization of products, regulatory approvals, dependence on key products, dependence on key customers and suppliers, and protection of intellectual property rights.

(E) Concentrations of Credit Risk:

Financial instruments that potentially subject the Company to concentration of credit risk include cash and cash equivalents. At March 31, 2021, substantially all of the cash balances are deposited in 2 banking institutions, each in excess of insured levels.

(F) Cash and Cash Equivalents:

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in money market funds.

(G) Property and Equipment:

Property and equipment, consisting of leasehold improvements, furniture and fixtures, computers, software and other office and laboratory equipment, is recorded at cost. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, retirement or sale, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation is recorded for property and equipment using the straight-line method over the estimated useful lives of the respective assets, generally three to five years, once the asset is installed and placed in service. Amortization of leasehold improvements is recorded over the shorter of the lease term or estimated useful life of the related asset.

The Company reviews the recoverability of all long-lived assets, including the related useful lives, whenever events or changes in circumstances indicate that the carrying amount of a long-lived asset might not be recoverable. Recoverability is measured by comparison of the book values of the assets to future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book value of the assets exceed their fair value, which is measured based on the projected discounted future net cash flows arising from the assets.

(H) Debt Issuance Costs and Debt Discount:

Debt issuance costs related to a recognized debt liability are presented on the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts, and are amortized to interest expense over the term of the related debt using the effective interest method. Further, debt discounts created as a result of the allocation of proceeds received from a debt issuance to warrants issued in conjunction with the debt issuance are amortized to interest expense under the effective interest method over the life of the recognized debt liability.

(I) Research and Development Expense:

Research and development costs are expensed as incurred. Clinical study costs are accrued over the service periods specified in the contracts and adjusted as necessary based upon an ongoing review of the level of effort and costs actually incurred. Payments for a product license prior to regulatory approval of the product and payments for milestones achieved prior to regulatory approval of the product are expensed in the period incurred as research and development. Milestone payments made in connection with final regulatory approvals are capitalized and amortized to cost of revenue over the remaining useful life of the asset. Research and development costs primarily consist of intellectual property and research and development materials acquired under license and license and collaboration agreements (see Note 3) and expenses from third parties who conduct research and development activities on behalf of the Company. The Company expenses in-process research and development projects acquired as asset acquisitions which have not reached technological feasibility, and which have no alternative future use.

(J) Income Taxes:

Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and the respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. A valuation allowance is recorded when, after consideration of all positive and negative evidence, it is not more likely than not that the Company's deferred tax assets will be realizable. 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. When and if the Company were to recognize interest and penalties related to unrecognized tax benefits, they would be reported in tax expense in the consolidated statement of operations.

(K) Stock-Based Compensation:

Stock-based awards to employees and directors with only time-based vesting requirements are valued at fair value on the date of grant and that fair value is recognized on a straight-line basis over the requisite service period of the entire award and is included in research and development expense and general and administrative expense in the Company's consolidated statements of operations. The Company values such time-based stock options using the Black-Scholes option pricing model. Certain assumptions are made with respect to utilizing the Black-Scholes option pricing model, including the expected life of the award, the volatility of the underlying shares and the risk-free interest rate. The expected life of such time-based stock options is calculated using the simplified method (based on the mid-point between the vesting date and the end of the contractual term), and the risk-free interest rate is based on the rates paid on securities issued by the U.S. Treasury with a term approximating the expected life of the equity award. The expected share price volatility for such time-based stock option awards was estimated partially using weighted average measures of implied volatility and using the average historical price volatility for industry peers.

The Company estimates the grant date fair value of stock option awards to employees with market-based performance conditions using a Monte Carlo Simulation method under the income approach. Certain assumptions are made with respect to utilizing the Monte Carlo Simulation method, including the volatility of the underlying shares and the drift rate, or estimated cost of equity. The expected share price volatility for such market-based performance stock option awards was estimated by taking the median historical price volatility for industry peers over the contractual term of the options. The drift rate, or estimated cost of equity, for such market-based performance stock option awards is based on various financial and risk-associated metrics of industry peers, as well as estimated factors specific to us.

The Company accounts for stock-based payments to nonemployees issued in exchange for services in accordance with ASU No. 2018-07, "*Compensation - Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*" based upon the fair value of the equity instruments issued. Compensation expense for stock options issued to nonemployees is calculated using the Black-Scholes option pricing model on the grant date and is recorded over the service performance period.

The Company recognizes forfeitures of awards when they occur.

(L) Net Loss per Share of Common Stock:

Basic net loss per share of common stock is computed by dividing the net loss applicable to shareholders of common stock by the weighted-average number of shares of common stock and 3,301,998 pre-funded warrants (see Note 9(B)) outstanding during the period, without further consideration for potentially dilutive securities. In accordance with ASC Topic 260, *Earnings Per Share*, the pre-funded warrants are included in the computation of basic net loss per share because the exercise price is negligible and they are fully vested and exercisable at any time after the original issuance date. Diluted net loss per share of common stock is computed by dividing the net loss applicable to shareholders of common stock by the diluted weighted-average number of shares of common stock outstanding during the period calculated in accordance with the treasury stock method. In periods in which the Company reports a net loss, all share of common stock equivalents are deemed anti-dilutive such that basic net loss per share of common stock and diluted net loss per share of common stock are equivalent. Potentially dilutive shares of common stock have been excluded from the diluted net loss per share of common stock computations in all periods presented because such securities have an anti-dilutive effect on net loss per share of common stock due to the Company’s net loss. There are no reconciling items used to calculate the weighted-average number of total shares of common stock outstanding for basic and diluted net loss per share of common stock data. Restricted Stock Units ("RSUs") and stock options outstanding for a total of 3.1 million and 2.3 million shares of common stock were not included in the calculation of diluted weighted-average shares of common stock outstanding for the years ended March 31, 2021 and 2020, respectively, because they were anti-dilutive given the net loss of the Company.

(M) Financial Instruments and Fair Value Measurement:

The Company utilizes fair value measurement guidance prescribed by accounting standards to value its financial instruments.

The guidance establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

Fair value is defined as the exchange price, or exit price, representing the amount that would be received from the sale of an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, the guidance establishes a three-tier fair value hierarchy that distinguishes among the following:

- Level 1-Valuations are based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access.
- Level 2-Valuations are based on quoted prices for similar assets or liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active and models for which all significant inputs are observable, either directly or indirectly.
- Level 3-Valuations are based on inputs that are unobservable (supported by little or no market activity) and significant to the overall fair value measurement.

To the extent the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The Company's financial instruments include cash and cash equivalents, a receivable from the sale of a long-term investment and long-term restricted cash. Cash consists of non-interest-bearing deposits denominated in the U.S. dollar, Swiss franc and Euro, while cash equivalents consists of interest-bearing money market fund deposits denominated in the U.S. dollar, which are invested in debt securities issued or guaranteed by the U.S. government and repurchase agreements fully collateralized by U.S. Treasury and U.S. government securities. Cash and the receivable from the sale of a long-term investment are stated at their respective historical carrying amounts, which approximate fair value due to their short-term nature. Long-term restricted cash is stated at its historical carrying amount, which approximates fair value. The carrying value of the Company's money market fund included in cash and cash equivalents of $114.0 million at March 31, 2021 approximated fair value, which is based on quoted prices in active markets for identical securities.

The following table summarizes the fair value of the Company's money market fund included in cash equivalents based on the inputs used at March 31, 2021 in determining such values (in thousands):

	Fair Value	Price Quotations (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market fund	$ 114,000	$ 114,000	$ —	$ —

(N) Recent Accounting Pronouncements:

In February 2016, the FASB issued ASU No. 2016-02, "*Topic 842 — Leases*" ("Topic 842"), which requires lessees to recognize on their consolidated balance sheets a liability to make lease payments and a right-of-use asset representing their right to use the underlying asset for the lease term for both finance and operating leases with lease terms greater than twelve months. Topic 842 is effective for annual periods beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2018. Early adoption is permitted. A modified retrospective transition approach is required, applying the new standard to all leases existing at the date of initial application. Topic 842 allows entities to choose to use either (i) the effective date or (ii) the beginning of the earliest comparative period presented in the financial statements as the date of initial application. Topic 842 provides a number of optional practical expedients in transition. The Company adopted Topic 842 on April 1, 2019 using the optional modified retrospective transition method. Comparative periods were not restated. For leases that commenced prior to April 1, 2019, the Company elected the following package of practical expedients when assessing the transition impact: (1) not to reassess whether any expired or existing contracts are or contain leases; (2) not to reassess the lease classification for any expired or existing leases; and (3) not to reassess initial direct costs for any existing leases. The Company also elected to: (1) use the total lease term in its initial incremental borrowing rate calculation; (2) combine its lease and non-lease components and account for them as a single lease component; and (3) not apply the use of hindsight in determining the lease term when considering lessee options to extend or terminate the lease and to purchase the underlying asset. Upon adoption, the Company recorded corresponding aggregate operating lease right-of-use assets and operating lease liabilities of $3.0 million and $2.4 million, respectively, including $0.6 million of prepaid rent previously classified within other non-current assets in the Company's consolidated balance sheet that was reclassified to operating lease right-of-use assets. The adoption of the new standard did not materially impact the Company's consolidated results of operations and cash flows and did not have an impact on the Company's beginning accumulated deficit balance. For additional information regarding the Company's leases, see Note 5 for further information regarding the impact of the Company's adoption of Topic 842.

In June 2016, the FASB issued ASU No. 2016-13, "*Financial Instruments — Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*" ("ASU No. 2016-13"). ASU 2016-13 requires that financial assets measured at amortized cost, such as loans, accounts and trade receivables and investments, be represented net of expected credit losses, which may be estimated based on relevant information such as historical experience, current conditions, and future expectation for each pool of similar financial asset. ASU No. 2016-13 requires enhanced disclosures related to trade receivables and associated credit losses. In May 2019, the FASB issued ASU No. 2019-05, "*Financial Instruments — Credit Losses (Topic 326): Targeted Transition Relief*", which allows for a transition election on certain instruments and is effective for Small Reporting Companies for fiscal years beginning after December 15, 2022 and interim periods in those fiscal years. In November 2019, the FASB issued ASU No. 2019-11, "*Codification Improvements to Topic 326, Financial Instruments — Credit Losses*", which amends certain aspects of ASU NO. 2016-13, including transition relief for trouble debt restructuring, among other topics. While the Company does not expect the adoption of this guidance to materially impact the Company's consolidated financial statements and related disclosures because it does not currently have any investments or trade receivables and the receivable from the sale of a long-term investment outstanding at March 31, 2021 was collected in May 2021, the impact on the Company's consolidated financial statements and disclosures will depend on the facts and circumstances of any specific future transactions.

In December 2019, the FASB issued ASU No. 2019-12, "*Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*" ("ASU No. 2019-12"). ASU No. 2019-12 simplifies the accounting for income taxes, eliminates certain exceptions within *Income Taxes (Topic 740)*, and clarifies certain aspects of the current guidance to promote consistency among reporting entities, and is effective for fiscal years, and for interim periods within those fiscal years, beginning after December 15, 2020, with early adoption permitted. Most amendments within ASU No. 2019-12 are required to be applied on a prospective basis, while certain amendments must be applied on a retrospective or modified retrospective basis. The Company early adopted the provisions of ASU No. 2019-12 on April 1, 2020, which did not have a material impact on its consolidated financial statements and related disclosures.

In August 2020, the FASB issued ASU No. 2020-06, "*Debt — Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging — Contracts in Entity's Own Equity (Subtopic 815-40)*" ("ASU No. 2020-06"). ASU No. 2020-06 simplifies the accounting for convertible debt instruments by removing the beneficial conversion and cash conversion separation models for convertible instruments. Under ASU No. 2020-06, the embedded conversion features are no longer separated from the host contract for convertible instruments with conversion features that are not required to be accounted for as derivatives or that do not result in substantial premiums accounted for as paid-in capital. ASU No. 2020-06 also amends the accounting for certain contracts in an entity's own equity that are currently accounted for as derivatives because of specific settlement provisions. In addition, the new guidance modifies how particular convertible instruments and certain contracts that may be settled in cash or shares impact the computation of diluted earnings or loss per share. The provisions of ASU No. 2020-06 are effective for fiscal years beginning after December 15, 2021, and interim periods within those fiscal years, with early adoption permitted, but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. While the Company does not expect the adoption of ASU No. 2020-06 to materially impact the Company's consolidated financial statements and related disclosures because it does not currently maintain any debt instruments accounted for in accordance with ASC Subtopic 470-20, "*Debt — Debt with Conversion and Other Options*" or instruments accounted for as derivatives in accordance with ASC Subtopic 815-40, "*Derivatives and Hedging — Contracts in Entity's Own Equity*", and the Company also currently includes outstanding pre-funded warrants in the computation of basic net loss per share (see Note 2(L)), the impact on the Company's consolidated financial statements and disclosures will depend on the facts and circumstances of any specific future transactions.

In May 2021, the FASB issued ASU No. 2021-04, "*Earnings Per Share (Topic 260), Debt — Modifications and Extinguishments (Subtopic 470-50), Compensation — Stock Compensation (Topic 718), and Derivatives and Hedging — Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options*" ("ASU No. 2021-04"). ASU No. 2021-04 provides a principles-based framework for issuers to account for a modification or exchange of freestanding equity-classified written call options. To the extent applicable, issuers first reference other U.S. GAAP to account for the effect of the modification. In the absence of other U.S. GAAP, ASU No. 2021-04 clarifies whether to account for the effect as an adjustment to equity, and the related EPS implications, or as an expense, and if so the manner and pattern of recognition. The provisions of ASU No. 2021-04 are effective for annual periods beginning after December 15, 2021, including interim periods within those fiscal years. Early adoption is permitted. While the Company does not expect the adoption of ASU No. 2021-04 to materially impact the Company's consolidated financial statements and related disclosures because it does not currently anticipate modifications to its outstanding equity-classified written call options, the impact on the Company's consolidated financial statements and disclosures will depend on the facts and circumstances of any specific future transactions.

Other recent accounting pronouncements issued by the FASB (including its Emerging Issues Task Force), the American Institute of Certified Public Accountants, and the SEC did not, or are not believed by management to, have a material impact on the Company's present or future consolidated financial position, results of operations or cash flows.

(O) Foreign Currency:

The Company has operations in the United States, the United Kingdom, Ireland and Switzerland. The results of its non-U.S. dollar based functional currency operations are translated to U.S. dollars at the average exchange rates during the year. The Company's assets and liabilities are translated using the current exchange rate as of the balance sheet date and shareholders' equity is translated using historical rates. Adjustments resulting from the translation of the financial statements of the Company's foreign functional currency subsidiaries into U.S. dollars are excluded from the determination of net loss and are accumulated in a separate component of shareholders' equity. Foreign exchange transaction gains and losses are included in other (income) expense in the Company's results of operations.

Note 3—License and Collaboration Agreements

(A) The University of Massachusetts Medical School Exclusive License Agreement:

In December 2018, the Company entered into an exclusive license agreement (the "UMMS Agreement"), with the University of Massachusetts Medical School ("UMMS") pursuant to which the Company received a worldwide, royalty-bearing, sub-licensable license under certain patent applications and any patents issuing therefrom, biological materials and know-how controlled by UMMS to develop and commercialize gene therapy product candidates, including AXO-AAV-GM1 and AXO-AAV-GM2, for the treatment of GM1 gangliosidosis and GM2 gangliosidosis (including Tay-Sachs disease and Sandhoff disease), respectively. This license is exclusive with respect to patents and biological materials and non-exclusive with respect to know-how and is subject to UMMS' retained rights for academic research, teaching and non-commercial patient care purposes, as well as to certain pre-existing rights of the U.S. government.

Under the UMMS Agreement, the Company is solely responsible, at its expense, for the research, development and commercialization of the licensed gene therapy product candidates. The Company will reimburse UMMS for payments made by UMMS for the manufacture of clinical trial materials for the Company, up to a specified amount. The Company is obligated to use diligent efforts to develop and commercialize the licensed gene therapy product candidates and is required to achieve certain development and commercial milestones in accordance with the timeline set forth in the agreement.

In addition, the Company could be obligated to make payments to UMMS totaling up to $24.5 million upon the achievement of specified development and regulatory milestones, including development and regulatory milestones of $1.0 million and $1.0 million that were achieved in February 2019 and October 2019, respectively, and that were paid during the fiscal year ended March 31, 2020, and up to $39.8 million upon the achievement of specified commercial milestones. The Company is also obligated to pay UMMS tiered mid-single digit royalties based on yearly net sales of the licensed products, subject to a specified annual minimum amount. Additionally, the Company will pay UMMS a percentage of any revenues it receives from any third-party sublicenses to licensed products at rates ranging in the mid-single digits to mid-teens.

Excluding development and regulatory milestones achieved, the Company incurred a total of $6.9 million and $8.8 million of program-specific costs related to its AXO-AAV-GM1 and AXO-AAV-GM2 programs within research and development expenses in its consolidated statements of operations during the years ended March 31, 2021 and March 31, 2020, respectively. The Company paid a total of $29 thousand and $3.0 million to UMMS during the years ended March 31, 2021 and March 31, 2020, respectively, including payments for development and regulatory milestones achieved.

The UMMS Agreement expires upon the expiration of the Company's obligations to make royalty payments to UMMS, which continues until the later of the expiration of licensed patents and any applicable orphan designation exclusivity and 10 years after the first commercial sale of the licensed products. Upon such expiration, the licenses granted to the Company by UMMS will automatically convert to perpetual, irrevocable, worldwide royalty-free licenses. The Company has the right to terminate the UMMS Agreement at any time upon 90 days' advance written notice to UMMS. Either party may terminate the UMMS Agreement for the other party's uncured material breach upon 60 days' advance written notice, including in the event that UMMS reasonably determines the Company has not fulfilled its diligence obligations.

(B) Oxford Biomedica License Agreement:

In 2018, the Company entered into an exclusive license agreement (the "Oxford Agreement") with Oxford Biomedica (UK) Ltd. ("Oxford"), pursuant to which the Company received a worldwide, exclusive, royalty-bearing, sub-licensable license under certain patents and other intellectual property controlled by Oxford to develop and commercialize AXO-Lenti-PD and related gene therapy products for all diseases and conditions. Under the terms of the Oxford Agreement, the Company could be obligated to make payments to Oxford totaling up to $55.0 million upon the achievement of specified development milestones, including certain development milestones that were achieved in April 2019 that resulted in a $13.0 million net payment due to Oxford that was paid during the year ended March 31, 2020, and up to $757.5 million upon the achievement of specified regulatory and sales milestones. The Company will also be obligated to pay Oxford a tiered royalty from 7% to 10%, based on yearly aggregate net sales of the underlying gene therapy products, subject to specified reductions upon the occurrence of certain events as set forth in the Oxford Agreement. These royalties are required to be paid, on a product-by-product and country-by-country basis, until the latest to occur of the expiration of the last to expire valid claim of a licensed patent covering such product in such country, the expiration of regulatory exclusivity for such product in such country, or 10 years after the first commercial sale of such product in such country.

The Company is solely responsible, at its expense, for all activities related to the development and commercialization of the gene therapy products underlying the Oxford Agreement. Pursuant to the Oxford Agreement, the Company is required to use commercially reasonable efforts to develop, obtain regulatory approval of, and commercialize a gene therapy product underlying the Oxford Agreement in the United States and at least one major market country in Europe. In addition, the Company is required to meet certain diligence milestones and to include at least one U.S.-based clinical trial site in a pivotal study of a gene therapy product underlying the Oxford Agreement. If the Company fails to meet any of these specified development milestones, it may cure such failure by paying Oxford certain fees, which range from $0.5 million to $1.0 million.

Excluding development milestones achieved, the Company incurred $5.7 million and $9.2 million of AXO-Lenti-PD program-specific costs within research and development expenses in its consolidated statement of operations during the years ended March 31, 2021 and March 31, 2020, respectively. The Company paid a total of $3.5 million and $15.2 million to Oxford during the years ended March 31, 2021 and March 31, 2020, respectively, including payments for development milestones achieved.

The Company has the right to terminate the Oxford Agreement at any time upon two months' advance written notice prior to the first commercial sale of a product, or for a specified period of advance written notice after the first commercial sale of a product. Either party may terminate the Oxford Agreement for the other party's uncured material breach or with respect to a failure to make a required payment.

(C) Benitec Biopharma License and Collaboration Agreement:

In July 2018, the Company entered into a license and collaboration agreement (the "Benitec Agreement") with Benitec Biopharma Limited ("Benitec"), pursuant to which the Company received a worldwide, exclusive, royalty-bearing, sub-licensable license under certain patents and other intellectual property controlled by Benitec to develop and commercialize investigational gene therapy AXO-AAV-OPMD and related gene therapy products (collectively, the "AXO-AAV-OPMD Program") for all diseases and conditions. The Company terminated the Benitec Agreement in its entirety, effective September 3, 2019. The Company incurred $1.8 million of AXO-AAV-OPMD Program-specific costs within research and development expenses in its consolidated statement of operations and paid a total of $2.8 million to Benitec during the year ended March 31, 2020.

Note 4—Investment in Arvelle Therapeutics B.V.

On February 13, 2019, the Company entered into a share subscription agreement (the "Subscription Agreement") to purchase up to approximately 8.1 million shares of nonredeemable convertible preferred stock of Arvelle Therapeutics B.V. in exchange for €0.00001 per share paid in cash, as well as certain goods and services provided by the Company to Arvelle. The Company accounted for its investment in Arvelle in accordance with the provisions of ASC 321, "*Investments - Equity Securities*", and elected to use the measurement alternative therein. The first closing under the Subscription Agreement occurred on February 25, 2019 with the Company purchasing approximately 5.9 million nonredeemable convertible preferred shares of Arvelle, which was initially recorded at a fair value of $5.9 million and was capitalized as a long-term investment in the Company's consolidated balance sheet and recorded to other non-operating income in its consolidated statement of operations. The Company also received the right to purchase up to approximately 2.2 million additional nonredeemable convertible preferred shares of Arvelle at a price of €0.00001 per share upon a potential future second closing under the Subscription Agreement. In May 2020, the Company fully exercised this right and purchased the approximately 2.2 million additional nonredeemable convertible preferred shares upon the closing of the second financing under the Subscription Agreement, which was recorded at a fair value of $2.2 million and was capitalized as a long-term investment in the Company's consolidated balance sheet and recorded to other non-operating income in the Company's consolidated statement of operations. In February 2021, the Company sold its investment in Arvelle to a third party as part of that third party's cash acquisition of all of the outstanding equity of Arvelle. In exchange, the Company received an upfront payment of approximately $11.6 million,in addition to a future payment to be received of approximately $1.2 million that is being held in escrow until August 2022 and that was recorded to long-term restricted cash in the Company's consolidated balance sheet at March 31, 2021, as well as the right to receive up to an additional total of $7.0 million in potential future regulatory and sales milestone payments (collectively, the "Arvelle Sale"). The Company recorded a net gain of approximately $4.7 million to other non-operating income in the Company's consolidated statement of operations upon the closing of the Arvelle Sale in February 2021, as well as a gain of approximately $4.3 million recorded to other non-operating income in the Company's consolidated statement of operations and to receivable from sale of long-term investment in its consolidated balance sheet upon the achievement of a regulatory milestone in March 2021.

Note 5—Leases

The Company adopted the provisions of Topic 842 on April 1, 2019 using the effective date as its date of initial application and applied the optional modified retrospective transition method. Comparative periods were not restated. For leases that commenced prior to April 1, 2019, the Company elected the following package of practical expedients when assessing the transition impact: (i) not to reassess whether any expired or existing contracts are or contain leases; (ii) not to reassess the lease classification for any expired or existing leases; and (iii) not to reassess initial direct costs for any existing leases. The Company also elected to: (i) use the total lease term in its initial incremental borrowing rate calculation; (ii) combine its lease and non-lease components and account for them as a single lease component; and (iii) not apply the use of hindsight in determining the lease term when considering lessee options to extend or terminate the lease and to purchase the underlying asset. Upon adoption, the Company recorded corresponding aggregate operating lease right-of-use assets and operating lease liabilities of $3.0 million and $2.4 million, respectively, including $0.6 million of prepaid rent previously classified within other non-current assets in the Company’s consolidated balance sheet that was reclassified to operating lease right-of-use assets. Operating right-of-use assets and obligations were recognized based on the present value of remaining lease payments over the lease term using an incremental borrowing rate of 12.9% upon adoption. As the Company’s operating leases do not provide an implicit rate, estimated incremental borrowing rates were used based on the information available at the adoption date in determining the present value of lease payments. Operating lease expense is recognized on a straight-line basis over the lease term. Variable lease costs such as common area costs and other operating costs are expensed as incurred. Leases with an initial term of 12 months or less are not recorded within the Company's balance sheet. In addition, the Company reviews agreements at inception to determine if they include a lease, and when they do, uses its incremental borrowing rate or implicit interest rate to determine the present value of the future lease payments.

In August 2020, the Company entered into a lease agreement for an office facility in New York, New York that commenced in December 2020 and ends in June 2026. Upon commencement of this lease, the Company recorded operating lease right-of-use assets and operating lease liabilities of approximately $1.1 million, net of expected abatement, based on the present value of payments over the lease term using an incremental borrowing rate of 8.9%. The Company also leases an office facility in Durham, North Carolina with a lease term ending in November 2022, and the Company had leased other office facilities in New York, New York and Princeton, New Jersey with lease terms that ended in January 2021 and October 2020, respectively. Each of these leases are or were, as applicable, classified as an operating lease in accordance with the provisions of Topic 842. The aggregate weighted-average remaining payment term, aggregate weighted-average remaining lease term and aggregate weighted-average discount rate were 5.0 years, 5.1 years and 9.2%, respectively, for the Company's contractual rent obligations for its operating leases as of March 31, 2021.

During the years ended March 31, 2021 and March 31, 2020, the Company incurred $1.6 million and $1.8 million, respectively, of rent expense associated with contractual rent obligations for its operating leases. During the years ended March 31, 2021 and March 31, 2020, the Company paid $0.9 million and $1.8 million, respectively, related to its contractual rent obligations. The following table provides a reconciliation of the Company's remaining undiscounted contractual rent obligations due within each respective fiscal year ending March 31 to the operating lease liabilities recognized as of March 31, 2021 (in thousands):

Year Ending March 31,	Amount
2022	$ 327
2023	272
2024	295
2025	303
2026	311
Thereafter	53
Total undiscounted payments	1,561
Less: present value adjustment	(318)
Present value of future payments	$ 1,243

Note 6—Accrued Expenses

As of March 31, 2021 and 2020, accrued expenses consisted of the following (in thousands):

	March 31, 2021	March 31, 2020
Research and development expenses	$ 6,091	$ 6,951
Bonuses and other compensation expenses	2,331	2,521
Legal expenses	15	704
Other expenses	759	1,143
Total accrued expenses	$ 9,196	$ 11,319

Note 7—Long-term Debt

In February 2017, the Company and certain of its subsidiaries (the "Borrowers") entered into a loan and security agreement (as amended in May 2017, September 2017 and November 2019) with Hercules Capital, Inc. ("Hercules") (the "Loan Agreement"), under which the Borrowers borrowed an aggregate of $55.0 million (the "Term Loan"). The Term Loan had a scheduled maturity date of March 1, 2021. The Term Loan initially bore interest at a variable per annum rate calculated for any day as the greater of either (i) the prime rate plus 6.80%, and (ii) 10.55%, which was subsequently changed in connection with the November 2019 amendment of the Loan Agreement to a variable per annum rate calculated for any day as the greater of either (i) the prime rate plus 6.80%, and (ii) 11.55%. The Borrowers were initially obligated to make monthly payments of accrued interest under the Loan Agreement until September 2018, followed by monthly installments of principal and interest from October 2018 until March 2021. Subsequent to the November 2019 amendment of the Loan Agreement, the Borrowers were obligated to make monthly payments of accrued interest from December 2019 until August 2020, followed by monthly installments of principal and interest from September 2020 until March 2021. Prepayment of the Term Loan was subject to penalty. The Company prepaid 50%, or approximately $15.7 million, of outstanding principal due without penalty in connection with the November 2019 amendment of the Loan Agreement, which was accounted for as a modification of debt in accordance with applicable accounting guidance. In April 2020, the Company prepaid $15.7 million of outstanding principal, together with $0.3 million of accrued interest, fees and other amounts, due under the Loan Agreement with Hercules, which was accounted for as an extinguishment of debt with a corresponding loss of approximately $0.5 million recorded to interest expense during the year ended March 31, 2021. In connection with the prepayment, the credit facility and the Loan Agreement with Hercules were terminated, and all obligations, liens and security interests under the Loan Agreement were released, discharged and satisfied.

Note 8—Related Party Transactions

(A) Services Agreements:

The Company has entered into services agreements with Roivant Sciences, Inc. ("RSI") and Roivant Sciences GmbH (collectively, the "Service Providers"), each a wholly owned subsidiary of RSL, pursuant to which the Service Providers provide the Company with services in relation to the identification of potential product candidates and project management of clinical trials, as well as other services related to the Company's development, administrative and financial functions (the "Services Agreements"). Under the terms of the Services Agreements, the Company is obligated to pay or reimburse the Service Providers for the costs they, or third parties acting on their behalf, incur in providing services to the Company, including administrative and support services as well as research and development services. In addition, the Company is obligated to pay to the Service Providers at a predetermined mark-up on any general and administrative and research and development services incurred directly by the Service Providers. Under the terms of the Services Agreements, the Service Providers have agreed to indemnify the Company and its officers, employees and directors against all losses arising out of, due to or in connection with the provision of services (or the failure to provide services) under the Services Agreements, subject to certain limitations set forth in the Service Agreements. In addition, the Company has agreed to indemnify the Service Providers and their respective affiliates and officers, employees and directors against all losses arising out of, due to or in connection with the receipt of services under the Services Agreements, subject to certain limitations set forth in the Services Agreements. Such indemnification obligations will not exceed the payments made by the Company under the Services Agreements for the specific service that allegedly caused or was related to the losses during the period in which such alleged losses were incurred. The term of each of the services agreements will continue until terminated upon 90 days' written notice by any party with respect to the services such party provides or receives thereunder. For the years ended March 31, 2021 and 2020, the Company incurred expenses of $0.1 million and $0.1 million, respectively, under the Services Agreements, inclusive of the mark-up, which have been treated as capital contributions (see Note 9(B)).

(B) Information Sharing and Cooperation Agreement:

In March 2015, the Company entered into an information sharing and cooperation agreement with RSL, as amended and restated in June 2018 (the "Restated Cooperation Agreement") in connection with a share purchase placement agreement with RSL (the "Private Placement"), for which the amendments became effective in July 2018 upon the closing of the Private Placement. The Restated Cooperation Agreement, among other things, obligates the Company to deliver periodic financial statements and other financial information to RSL and comply with other specified financial reporting requirements, and requires the Company to implement and observe certain policies and procedures related to applicable laws and regulations. The Company agreed to indemnify RSL and its affiliates and their respective officers, employees and directors against all losses arising out of, due to or in connection with RSL's status as a shareholder under the Restated Cooperation Agreement and the operations of or services provided by RSL or its affiliates or their respective officers, employees or directors to the Company or any of its subsidiaries, subject to certain limitations set forth in the Restated Cooperation Agreement.

Subject to specified exceptions, the Restated Cooperation Agreement will terminate at such time as RSL is no longer required (a) under U.S. GAAP to consolidate the Company's results of operations and financial position, (b) under U.S. GAAP to account for its investment in the Company under the equity method of accounting, or (c) otherwise to include separate financial statements of the Company in its filings with the SEC pursuant to any SEC rule. In addition, the Cooperation Agreement may be terminated upon mutual written consent of the parties or upon written notice from RSL to the Company in the event of the Company's bankruptcy, liquidation, dissolution or winding-up.

(C) RSL Financing Participation:

In February 2020, the Company issued and sold 16,631,336 shares of common stock and pre-funded warrants to purchase up to 3,301,998 shares of common stock in a follow-on public offering, including 2,600,000 shares of common stock sold pursuant to the exercise of the underwriters' option to purchase additional shares and also including 5,333,333 shares of common stock issued and sold to RSL, at an offering price of $3.75 per share of common stock and $3.74999 per pre-funded warrant. The net proceeds to the Company were approximately $70.8 million, after deducting underwriting discounts and commissions and offering expenses incurred (see Note 9(B)).

Note 9—Stockholders' Equity

(A) Overview:

Sio's Certificate of Incorporation filed with the State of Delaware on November 12, 2020 authorizes the issuance of up to a total of 1,010,000,000 shares, of which 1,000,000,000 shares are common stock with a par value of $0.00001 per share and 10,000,000 shares are preferred stock with a par value of $0.00001 per share. A 1-for-8 reverse stock split of the Company's outstanding common stock was effected in May 2019 as approved by the Company's Board of Directors and a majority of its shareholders. As such, all references to share and per share amounts in these consolidated financial statements and accompanying notes have been retroactively restated to reflect the 1-for-8 reverse stock split, except for the authorized number of shares of the Company's common stock and the par value per share, which were not affected. The reverse stock split reduced the number of the Company's shares of common stock issued and outstanding from approximately 182.2 million to 22.8 million as of March 31, 2019.

(B) Transactions:

During the years ended March 31, 2021 and March 31, 2020, expenses of $0.1 million and $0.1 million, respectively, of expenses were incurred by RSI on behalf of the Company and were recorded as capital contributions (see Note 8(A)).

In February 2020, the Company issued and sold 16,631,336 shares of common stock and pre-funded warrants to purchase up to 3,301,998 shares of common stock in a follow-on public offering, including 2,600,000 shares of common stock sold pursuant to the exercise of the underwriters' option to purchase additional shares and also including 5,333,333 shares of common stock issued and sold to RSL, at an offering price of $3.75 per share of common stock and $3.74999 per pre-funded warrant. The net proceeds to the Company were approximately $70.8 million, after deducting underwriting discounts and commissions and offering expenses incurred (see Note 8(C)). The pre-funded warrants do not expire and are immediately exercisable except that the pre-funded warrants cannot be exercised by the holder if, after giving effect thereto, the holder would beneficially own more than 9.99% of the Company's common stock, subject to certain exceptions. The pre-funded warrants are classified as equity in accordance with ASC 480, "*Distinguishing Liabilities from Equity*", and the fair value of the pre-funded warrants was recorded as a credit to additional paid-in capital and is not subject to remeasurement. As of March 31, 2021, none of the pre-funded warrants had been exercised.

During the year ended March 31, 2021, the Company engaged SVB Leerink LLC as its agent to sell shares of the Company's common stock from time to time through an at-the-market equity offering program. SVB Leerink LLC receives compensation for its services in an amount equal to 3% of the gross proceeds of any of the Company's common stock sold. As of March 31, 2021, the Company sold approximately 29.7 million shares of its common stock for total proceeds of approximately $90.5 million, net of brokerage fees, under this program, and subsequent to March 31, 2021, the Company has sold approximately 0.2 million shares of its common stock for total proceeds of approximately $0.5 million, net of brokerage fees (see Note 14).

Note 10—Stock-Based Compensation

(A) Amended and Restated 2015 Equity Incentive Plan:

In March 2015, the Company adopted its 2015 Equity Incentive Plan, which was amended and restated in June 2017 by its Board of Directors and became effective upon shareholder approval in August 2017 and was further amended and restated by the Company's Board of Directors in October 2020 (the "2015 Plan"). A 1-for-8 reverse stock split of the Company's outstanding common stock was effected on in 2019 as approved by the Company's Board of Directors and a majority of its shareholders. As such, all references to share and per share amounts in these consolidated financial statements and accompanying notes have been retroactively restated to reflect the 1-for-8 reverse stock split, except for the authorized number of shares of the Company's common stock and the par value per share, which were not affected. The reverse stock split reduced each of (i) the number of shares authorized for issuance from 24.8 million to 3.1 million, (ii) the number of shares available for issuance from 8.4 million to 1.0 million, and (iii) the number of options outstanding from 15.4 million to 1.9 million under the 2015 Plan as of March 31, 2019. In April 2019 and April 2020, the number of shares of common stock authorized for issuance under the 2015 Plan increased automatically by 0.9 million and 1.6 million, respectively, in accordance with the terms of the 2015 Plan. At March 31, 2021, totals of 5.6 million shares of common stock were authorized for issuance and 2.0 million shares of common stock were available for future issuance under the 2015 Plan.

(B) Stock Options:

Stock options granted under the 2015 Plan provide option holders, if approved by the Board of Directors, the right to exercise their options prior to vesting. In the event that an option holder exercises the unvested portion of any option, such unvested portion will be subject to a repurchase option held by the Company at the lower of (i) the fair market value of its common stock on the date of repurchase and (ii) the exercise price of the options. Any shares of common stock underlying such unvested portion will continue to vest in accordance with the original vesting schedule of the option.

Time-based stock options granted to the Company's employees vest over a period of four years with 25% of the shares of common stock underlying the option vesting on the first anniversary of the vesting commencement date and the remainder vesting in 12 quarterly installments thereafter, subject to continuing service. Initial stock options granted to the Company's non-employee directors vest in equal installments on the first, second and third anniversaries of the vesting commencement date, and stock options subsequently granted annually to the Company's non-employee directors vest fully on the first anniversary of the vesting commencement date, each subject to continuous service. Stock options granted to employees during the year ended March 31, 2020 include options with market-based performance conditions to purchase 0.4 million shares of common stock with a weighted average exercise price of $8.07 per share and a corresponding total estimated grant date fair value of $1.2 million, which was estimated using Monte Carlo Simulation method under the income approach. The Company did not grant any market-based performance stock options during the year ended March 31, 2021. At March 31, 2021, options with market-based performance conditions to purchase 0.4 million shares of common stock at a weighted average exercise price of $8.87 per share were outstanding. The market-based performance options vest based on the trading price for the Company's shares of common stock exceeding certain closing price thresholds.

The Company estimated the fair value of each time-based stock option on the date of grant using the Black-Scholes closed-form option-pricing model applying the weighted average assumptions during the years ended March 31, 2021 and March 31, 2020, as follows:

	Years Ended March 31,	
	2021	2020
Expected stock price volatility	109.5 %	78.9 %
Expected risk free interest rate	0.43 %	2.30 %
Expected term, in years	6.11	6.13
Expected dividend yield	— %	— %

The Company estimated the grant date fair value of each market-based performance stock option granted during the year ended March 31, 2020 using a Monte Carlo Simulation method under the income approach by applying the following assumptions:

Expected share price volatility	73.6 - 74.3%
Contractual term, in years	10

The following table presents a summary of stock option activity and data under the 2015 Plan:

	Number of Options	Weighted Average Exercise Price	Weighted Average Grant Date Fair Value	Weighted Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value
Options outstanding at March 31, 2019	1,919,158	$ 34.09	$ 49.35	6.86	$ 1,569,809
Granted	1,541,672	8.12	4.96		
Exercised	(11,778)	7.20	114.40		2,972
Forfeited	(1,440,317)	33.99	50.32		
Options outstanding at March 31, 2020	2,008,735	$ 14.39	$ 13.87	8.33	$ —
Granted	434,775	3.72	3.07		
Exercised	—	—	—		—
Forfeited	(347,967)	13.92	15.84		
Options outstanding at March 31, 2021	2,095,543	$ 12.26	$ 11.30	7.90	$ —
Options vested and expected to vest at March 31, 2021	2,095,543	$ 12.26	$ 11.30	7.90	$ —
Options exercisable at March 31, 2021	1,571,191	$ 14.77	$ 13.78	7.59	$ —

During the years ended March 31, 2021 and March 31, 2020, the total grant date fair values of options that vested under the 2015 Plan were $3.5 million and $3.8 million, respectively. At March 31, 2021 under the 2015 Plan, vested options to purchase a total of 0.9 million shares of common stock were outstanding, with no options with market-based performance conditions vested and outstanding.

(C) Restricted Stock Units:

Of the total number of RSUs granted in September 2019 representing approximately 0.3 million shares of the Company's common stock, one-half vested on January 31, 2020 and the remaining one-half vested on July 31, 2020, subject to continuing service. All other RSUs granted during the years ended March 31, 2021 and March 31, 2020 vest in three equal annual installments commencing on the first anniversary of the vesting commencement date, subject to continuing service.

The following table presents a summary of restricted stock unit activity and data under the 2015 Plan:

	Number of RSUs	Weighted Average Grant Date Fair Value
RSUs outstanding at March 31, 2019	—	$ —
Granted	369,577	7.50
Vested and settled	(103,294)	7.77
Forfeited	(18,420)	7.77
RSUs outstanding at March 31, 2020	247,863	$ 7.37
Granted	1,247,850	3.37
Vested and settled	(187,741)	7.68
Forfeited	(281,756)	3.95
RSUs outstanding at March 31, 2021	1,026,216	$ 3.39

During the years ended March 31, 2021 and March 31, 2020, the total grant date fair values of RSUs that vested under the 2015 Plan were $1.0 million and $1.2 million, respectively. All 1.0 million of the RSUs outstanding at March 31, 2021 were unvested, and approximately 0.2 million of the RSUs outstanding at March 31, 2020 were unvested.

(D) Stock-based Compensation Expense:

The Company recorded total stock-based compensation expense of $4.4 million and $7.0 million for the years ended March 31, 2021 and March 31, 2020, respectively, related to options and RSUs granted to its employees and directors, excluding stock-based compensation expense allocated to the Company from RSL (see Note 10(E)). At March 31, 2021, total unrecognized compensation expense for unvested outstanding option and RSU equity awards of the Company's common stock granted to its employees and directors under the 2015 Plan was $6.2 million, which is expected to be recognized over the remaining weighted-average service period of 2.16 years.

(E) RSL Common Share Awards and Options:

Certain employees of the Company, as well as certain employees of RSL and certain of its subsidiaries, have been granted RSL common share awards and options for which stock-based compensation expense is allocated to the Company from RSL. The Company recorded such total allocated stock-based compensation expense of $0.1 million and $0.9 million during the years ended March 31, 2021 and March 31, 2020, respectively.

Note 11—Income Taxes

The loss before income taxes and the related tax expense are as follows (in thousands):

	Year ended March 31, 2021	Year ended March 31, 2020
Loss before income taxes:		
United States	$ (17,382)	$ (4,403)
Switzerland [1]	(11,978)	(62,520)
Bermuda [2]	(3,177)	(5,216)
Other [3]	(100)	(51)
Total loss before income taxes	$ (32,637)	$ (72,190)
Current taxes:		
United States	$ (212)	$ 403
Switzerland [1]	—	—
Bermuda [2]	—	—
Other [4]	—	35
Total current tax expense	(212)	438
Deferred taxes:		
United States	—	—
Switzerland [1]	—	—
Bermuda [2]	—	—
Other [3]	—	—
Total deferred tax expense	—	—
Total income tax expense	$ (212)	$ 438

[1] Wholly-owned subsidiary, Axovant Sciences GmbH.

[2] Bermuda entity was centrally controlled and managed in the United Kingdom.

[3] Wholly-owned subsidiaries, Axovant Holdings Limited (United Kingdom) and Sio Europe Limited (Ireland).

[4] Includes state income tax expense.

A reconciliation of income tax benefit computed at the U.S/Bermuda statutory rate to income tax (benefit) expense reflected in the financial statements is as follows (in thousands):

	Year Ended March 31, 2021		Year Ended March 31, 2020	
	$	%	$	%
Income tax benefit at federal statutory rate	$ (6,854)	21.00 %	$ —	— %
Foreign rate differential [1]	1,118	(3.43)	(17,268)	23.92
Nondeductible/nontaxable items	(1,823)	5.59	766	(1.06)
Valuation allowance	10,749	(32.94)	16,759	(23.21)
Research and development credit	(914)	2.80	(615)	0.85
Research and development true-up	(301)	0.92	(285)	0.39
Deferred adjustments	2,139	(6.55)	1,068	(1.48)
Restructuring	(4,108)	12.59	—	—
Other	(218)	0.67	13	(0.02)
Total income tax (benefit) expense	$ (212)	0.65 %	$ 438	(0.61)%

[1] Primarily related to current tax on United States operations including permanent and temporary differences, Swiss net operating losses and United Kingdom taxation of the parent company.

Until November 12, 2020, the Company was not subject to taxation under the laws of Bermuda since AGT was organized as a Bermuda Exempted Limited Company, for which there is no current tax regime. Since November 12, 2020, when Sio was incorporated in the State of Delaware in connection with the Domestication (see Note 1), the Company is subject to taxation under the laws of the United States of America. The Company's provision for income taxes is primarily federal, state and local taxes in the United States. The Company's effective tax rates of 0.65% and (0.61)% for the years ended March 31, 2021 and March 31, 2020, respectively, differ from the U.S. federal statutory rate of 21% and the Bermuda federal statutory rate of 0% primarily due to the U.S. permanent unfavorable tax differences, stock compensation deductions and a valuation allowance that effectively eliminates the Company's net deferred tax assets.

On March 27, 2020, the United States government enacted the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act") which includes numerous modifications to income tax provisions, including a limitation on business interest expense and net operating loss provisions and the acceleration of alternative minimum tax credits. Given the Company's history of losses, the CARES Act is not expected to have a material impact on its income tax positions.

As of March 31, 2021, the Company had an aggregate tax receivable of $1.7 million from various federal, state and local jurisdictions. Deferred taxes reflect the tax effects of the differences between the amounts recorded as assets and liabilities for financial reporting purposes and the comparable amounts recorded for income tax purposes. Significant components of the deferred tax assets (liabilities) at March 31, 2021 and 2020 are as follows (in thousands):

	March 31, 2021	March 31, 2020
Deferred tax assets:		
Net operating loss	$ 154,877	$ 160,319
Research tax credits	11,798	10,782
Stock-based compensation	8,341	10,738
Intangibles	8,747	6,738
Lease liability	257	206
Other	51	78
Subtotal	184,071	188,861
Valuation allowance	(183,703)	(187,762)
Deferred tax liabilities:		
Right of use	(250)	(334)
Other	(118)	(765)
Total net deferred tax assets	$ —	$ —

The Company had net operating losses in the United States, Switzerland, the United Kingdom and Ireland in the amounts of $3.2 million, $1.18 billion, $150 thousand and $77 thousand, respectively, as of March 31, 2021. The United States federal net operating loss can be carried forward indefinitely with utilization limited to 80% of future taxable income for tax years beginning after January 1, 2021. The Switzerland net operating loss will begin to expire as of March 31, 2025. The United Kingdom net operating loss can be carried forward indefinitely with an annual limitation on utilization. As of March 31, 2021, the Company has federal research and development carryforwards of approximately $11.8 million. If not utilized, the research and development credit carryforwards will start to expire in 2038.

The Company assesses the realizability of the deferred tax assets at each balance sheet date based on available positive and negative evidence in order to determine the amount which is more likely than not to be realized and record a valuation allowance as necessary. Due to the Company's cumulative loss position which provides significant negative evidence difficult to overcome, the Company has recorded a full valuation allowance of $183.7 million as of March 31, 2021, representing the portion of the deferred tax asset that is not more likely than not to be realized. The Company will continue to assess the realizability of deferred tax assets at each balance sheet date in order to determine the proper amount, if any, required for a valuation allowance.

As of March 31, 2021, the Company does not have unremitted earnings from foreign subsidiaries. The potential tax implications of the repatriation of unremitted earnings are driven by the facts at the time of distribution; however, due to U.S. tax reform and the Company’s current accumulated earnings deficit, the incremental cost to repatriate earnings is not expected to be material.

The Company is subject to tax and files income tax returns in the United Kingdom, Switzerland, Ireland and the United States federal and United States state and local jurisdictions. The Company is subject to tax examinations for tax years ended March 31, 2016 and forward in all applicable income tax jurisdictions. Tax audits and examinations can involve complex issues, interpretations and judgments. The resolution of matters may span multiple years particularly if subject to litigation or negotiation. The Company believes it has appropriately recorded its tax position using reasonable estimates and assumptions, however the potential tax benefits may impact the results of operations or cash flows in the period of resolution, settlement or when the statutes of limitations expire. There are no unrecognized tax benefits recorded as of March 31, 2021.

Note 12—Commitments and Contingencies

As of March 31, 2021, the Company had entered into commitments under the UMMS Agreement (see Note 3(A)), the Oxford Agreement (see Note 3(B)), the Services Agreements with certain of RSL's wholly owned subsidiaries (see Note 8(A)) and agreements to rent office space (see Note 5). In addition, the Company has entered into services agreements with third parties for pharmaceutical manufacturing and research activities in the normal course of business, which can generally be terminated by the Company with 30- or 60-days' written notice, unless otherwise indicated. Further, certain of the Company's manufacturing agreements could require early termination and wind-down payments due from the Company upon either the termination of its clinical trials or if the Company terminates such agreements for convenience.

The Company has the right to terminate the UMMS Agreement at any time upon 90 days' advance written notice to UMMS. Either party may terminate the UMMS Agreement for the other party's uncured material breach upon 60 days' advance written notice, including in the event that UMMS reasonably determines the Company has not fulfilled its diligence obligations.

The Company has the right to terminate the Oxford Agreement at any time upon two months' advance written notice prior to the first commercial sale of a product, or for a specified period of advance written notice after the first commercial sale of a product. Either party may terminate the Oxford Agreement for the other party's uncured material breach or with respect to a failure to make a required payment.

Note 13—Selected Quarterly Financial Data (Unaudited)

The following table presents selected quarterly financial data for the years ended March 31, 2021 and March 31, 2020 (in thousands, except per share amounts):

	First Quarter Ended June 30, 2020	Second Quarter Ended September 30, 2020	Third Quarter Ended December 31, 2020	Fourth Quarter Ended March 31, 2021	First Quarter Ended June 30, 2019	Second Quarter Ended September 30, 2019	Third Quarter Ended December 31, 2019	Fourth Quarter Ended March 31, 2020
Research and development expenses	$ 5,194	$ 5,058	$ 6,407	$ 8,244	$ 21,090	$ 6,833	$ 8,267	$ 10,920
General and administrative expenses	4,640	4,491	4,198	3,965	6,468	5,051	5,409	5,133
Total operating expenses	9,834	9,549	10,605	12,209	27,558	11,884	13,676	16,053
Net loss	(8,594)	(9,984)	(10,516)	(3,331)	(28,057)	(13,884)	(14,039)	(16,648)
Net loss per share attributable to shareholders of common stock - basic and diluted	$ (0.20)	$ (0.21)	$ (0.20)	$ (0.05)	$ (1.23)	$ (0.61)	$ (0.62)	$ (0.54)

Note 14—Subsequent Events

Subsequent to March 31, 2021, the Company has sold approximately 0.2 million shares of its common stock for total proceeds of approximately $0.5 million, net of brokerage fees, through SVB Leerink LLC as placement agent.