

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

FORM 10-Q

(Mark One)

- QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the quarterly period ended December 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

(State or other jurisdiction of
incorporation or organization)

130 West 42nd St., 26th Floor, New York, NY
(Address of principal executive offices)

85-3863315

(I.R.S. Employer
Identification No.)

10036
(Zip Code)

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

N/A

(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 (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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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

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

The number of shares outstanding of the Registrant's common stock, \$0.00001 par value per share, on February 8, 2022, was 73,705,444.

SIO GENE THERAPIES INC.
QUARTERLY REPORT ON FORM 10-Q
FOR THE QUARTER ENDED DECEMBER 31, 2021

TABLE OF CONTENTS

	<u>Page</u>
<u>PART I. FINANCIAL INFORMATION</u>	
<u>Item 1. Financial Statements (Unaudited):</u>	
<u>Condensed Consolidated Balance Sheets as of December 31, 2021 and March 31, 2021</u>	5
<u>Condensed Consolidated Statements of Operations for the Three and Nine-Months Ended December 31, 2021 and 2020</u>	6
<u>Condensed Consolidated Statements of Comprehensive Loss for the Three and Nine-Months Ended December 31, 2021 and 2020</u>	7
<u>Condensed Consolidated Statements of Stockholders' Equity for the Three and Nine-Months Ended December 31, 2021 and 2020</u>	8
<u>Condensed Consolidated Statements of Cash Flows for the Nine Months Ended December 31, 2021 and 2020</u>	10
<u>Notes to Condensed Consolidated Financial Statements</u>	11
<u>Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	19
<u>Item 3. Quantitative and Qualitative Disclosures About Market Risk</u>	29
<u>Item 4. Controls and Procedures</u>	29
<u>PART II. OTHER INFORMATION</u>	
<u>Item 1. Legal Proceedings</u>	30
<u>Item 1A. Risk Factors</u>	31
<u>Item 2. Unregistered Sales of Equity Securities and Use of Proceeds</u>	79
<u>Item 3. Defaults Upon Senior Securities</u>	79
<u>Item 4. Mine Safety Disclosures</u>	79
<u>Item 5. Other Information</u>	79
<u>Item 6. Exhibits</u>	80
<u>SIGNATURES</u>	81

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 development. If we are unable to successfully develop and commercialize any of our product candidates, our business will be harmed.
- 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.
- 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 have previously resulted, and may in the future 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 II, Item 1A, and the other information set forth in this Quarterly Report on Form 10-Q, including our unaudited condensed 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. FINANCIAL INFORMATION
Item 1. Financial Statements (Unaudited)

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

	December 31, 2021	March 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 81,910	\$ 118,986
Restricted cash	1,184	—
Receivable from sale of long-term investment	—	4,343
Prepaid expenses and other current assets	5,244	7,348
Income tax receivable	1,732	1,656
Total current assets	90,070	132,333
Long-term restricted cash	—	1,184
Operating lease right-of-use assets	2,613	1,152
Property and equipment, net	623	478
Total assets	\$ 93,306	\$ 135,147
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 6,611	\$ 1,341
Accrued expenses	7,762	9,196
Current portion of operating lease liabilities	765	311
Total current liabilities	15,138	10,848
Operating lease liabilities, net of current portion	1,903	932
Total liabilities	17,041	11,780
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Common stock, par value \$0.00001 per share, 1,000,000,000 shares authorized, 73,697,110 and 69,377,567 issued and outstanding at December 31, 2021 and March 31, 2021, respectively	1	1
Additional paid-in capital	925,558	914,100
Accumulated deficit	(849,632)	(791,069)
Accumulated other comprehensive income	338	335
Total stockholders' equity	76,265	123,367
Total liabilities and stockholders' equity	\$ 93,306	\$ 135,147

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

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

	Three Months Ended December 31,		Nine Months Ended December 31,	
	2021	2020	2021	2020
Operating expenses:				
Research and development expenses				
(includes stock-based compensation expense of \$130 and \$259 for the three months ended December 31, 2021 and 2020, respectively, and \$1,051 and \$1,280 for the nine months ended December 31, 2021 and 2020, respectively)	\$ 21,287	\$ 6,407	\$ 40,793	\$ 16,659
General and administrative expenses				
(includes stock-based compensation expense of \$1,268 and \$617 for the three months ended December 31, 2021 and 2020, respectively, and \$8,966 and \$2,294 for the nine months ended December 31, 2021 and 2020, respectively)	4,086	4,198	17,693	13,329
Total operating expenses	25,373	10,605	58,486	29,988
Other expenses (income):				
Interest expense	7	1	19	798
Other expense (income)	76	98	86	(1,388)
Loss before income tax benefit	(25,456)	(10,704)	(58,591)	(29,398)
Income tax benefit	—	(188)	(28)	(304)
Net loss	\$ (25,456)	\$ (10,516)	\$ (58,563)	\$ (29,094)
Net loss per share of common stock — basic and diluted	\$ (0.35)	\$ (0.20)	\$ (0.80)	\$ (0.61)
Weighted-average shares of common stock outstanding — basic and diluted	73,335,279	52,679,816	73,046,889	47,581,795

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

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

	Three Months Ended December 31,		Nine Months Ended December 31,	
	2021	2020	2021	2020
Net loss	\$ (25,456)	(10,516)	\$ (58,563)	(29,094)
Other comprehensive income:				
Foreign currency translation adjustment	1	6	3	398
Total other comprehensive income	1	6	3	398
Comprehensive loss	<u>\$ (25,455)</u>	<u>\$ (10,510)</u>	<u>\$ (58,560)</u>	<u>\$ (28,696)</u>

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

SIO GENE THERAPIES INC.
Condensed Consolidated Statements of Stockholders' Equity
(Unaudited, in thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount				
Balance at March 31, 2020	39,526,299	\$ —	\$ 820,257	\$ (758,644)	\$ (55)	\$ 61,558
Shares issued upon settlement of restricted stock units	53,653	—	—	—	—	—
Shares sold in connection with at-the-market offering, net of brokerage fees and offering expenses of \$0.5 million	1,393,428	—	3,930	—	—	3,930
Stock-based compensation expense	—	—	1,590	—	—	1,590
Capital contribution received from affiliate	—	—	53	—	—	53
Foreign currency translation adjustment	—	—	—	—	44	44
Net loss	—	—	—	(8,594)	—	(8,594)
Balance at June 30, 2020	40,973,380	\$ —	\$ 825,830	\$ (767,238)	\$ (11)	\$ 58,581
Shares issued upon settlement of restricted stock units	60,676	—	—	—	—	—
Shares sold in connection with at-the-market offering, net of brokerage fees and offering expenses of \$0.7 million	6,215,673	—	19,598	—	—	19,598
Stock-based compensation expense	—	—	1,108	—	—	1,108
Capital contribution received from affiliate	—	—	22	—	—	22
Foreign currency translation adjustment	—	—	—	—	348	348
Net loss	—	—	—	(9,984)	—	(9,984)
Balance at September 30, 2020	47,249,729	\$ —	\$ 846,558	\$ (777,222)	\$ 337	\$ 69,673
Shares issued upon settlement of restricted stock units	7,334	—	—	—	—	—
Shares sold in connection with at-the-market offering, net of brokerage fees and offering expenses of \$1.1 million	9,345,563	1	28,985	—	—	28,986
Stock-based compensation expense	—	—	876	—	—	876
Capital contribution received from affiliate	—	—	4	—	—	4
Foreign currency translation adjustment	—	—	—	—	6	6
Net loss	—	—	—	(10,516)	—	(10,516)
Balance at December 31, 2020	56,602,626	\$ 1	\$ 876,423	\$ (787,738)	\$ 343	\$ 89,029

SIO GENE THERAPIES INC.
Condensed Consolidated Statements of Stockholders' Equity
(Unaudited, in thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount				
Balance at March 31, 2021	69,377,567	\$ 1	\$ 914,100	\$ (791,069)	\$ 335	\$ 123,367
Shares issued upon settlement of restricted stock units	82,542	—	—	—	—	—
Shares sold in connection with at-the-market offering, net of brokerage fees and offering expenses of \$0.0 million	179,400	—	479	—	—	479
Stock-based compensation expense	—	—	1,321	—	—	1,321
Foreign currency translation adjustment	—	—	—	—	2	2
Net loss	—	—	—	(11,870)	—	(11,870)
Balance at June 30, 2021	69,639,509	\$ 1	\$ 915,900	\$ (802,939)	\$ 337	\$ 113,299
Shares issued upon exercise of pre-funded warrants	3,301,998	—	—	—	—	—
Stock-based compensation expense	—	—	7,298	—	—	7,298
Net loss	—	—	—	(21,237)	—	(21,237)
Balance at September 30, 2021	72,941,507	\$ 1	\$ 923,198	\$ (824,176)	\$ 337	\$ 99,360
Shares issued upon settlement of restricted stock units	195,558	—	—	—	—	—
Shares sold in connection with at-the-market offering, net of brokerage fees and offering expenses of \$0.2 million	560,045	—	962	—	—	962
Stock-based compensation expense	—	—	1,398	—	—	1,398
Foreign currency translation adjustment	—	—	—	—	1	1
Net loss	—	—	—	(25,456)	—	(25,456)
Balance at December 31, 2021	73,697,110	\$ 1	\$ 925,558	\$ (849,632)	\$ 338	\$ 76,265

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

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

	Nine Months Ended December 31,	
	2021	2020
Cash flows from operating activities:		
Net loss	\$ (58,563)	\$ (29,094)
Adjustments to reconcile net loss to net cash used in operating activities:		
Amortization of operating lease right-of-use assets	229	1,326
Stock-based compensation expense	10,017	3,574
Depreciation and non-cash amortization expense	187	851
Gain on long-term investment	—	(2,184)
Change in operating lease liabilities	(265)	(883)
Other	7	440
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	2,104	(3,301)
Income tax receivable	(76)	21
Other non-current assets	—	(76)
Accounts payable	5,270	(3,425)
Accrued expenses	(1,434)	(3,597)
Net cash used in operating activities	(42,524)	(36,348)
Cash flows from investing activities:		
Cash proceeds from sale of long-term investment	4,343	—
Purchases of property and equipment	(336)	(247)
Net cash provided by (used in) investing activities	4,007	(247)
Cash flows from financing activities:		
Payments on long-term debt	—	(15,731)
Capital contributions received from affiliate	—	79
Cash proceeds from issuance of shares of common stock, net of issuance costs	1,441	52,514
Net cash provided by financing activities	1,441	36,862
Net change in cash and cash equivalents, restricted cash and long-term restricted cash	(37,076)	267
Total cash and cash equivalents, restricted cash and long-term restricted cash—beginning of period	120,170	80,752
Total cash and cash equivalents, restricted cash and long-term restricted cash—end of period	\$ 83,094	\$ 81,019
Cash and cash equivalents—beginning of period	118,986	80,752
Restricted cash included in long-term assets—beginning of period	1,184	—
Total cash and cash equivalents, restricted cash and long-term restricted cash—beginning of period	\$ 120,170	\$ 80,752
Cash and cash equivalents—end of period	81,910	81,019
Restricted cash included in current assets—end of period	1,184	—
Total cash and cash equivalents, restricted cash and long-term restricted cash—end of period	\$ 83,094	\$ 81,019
Non-cash operating activities:		
Operating lease right-of-use assets and operating lease liabilities recognized	\$ 1,690	\$ 1,141

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

SIO GENE THERAPIES INC.
Notes to Condensed Consolidated Financial Statements (Unaudited)

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 and GM2 gangliosidosis (including Tay-Sachs and Sandhoff diseases). 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 unaudited condensed consolidated financial statements and accompanying notes have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP") for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and disclosures required by U.S. GAAP for complete financial statements. These unaudited condensed consolidated financial statements and accompanying notes should be read in conjunction with the Company's audited consolidated financial statements and notes thereto included in the Company's Annual Report on Form 10-K for the fiscal year ended March 31, 2021 (the "Annual Report"), filed with the SEC on June 9, 2021. In the opinion of management, all adjustments (consisting of normal recurring adjustments) considered necessary to present fairly the financial position of the Company and its results of operations and cash flows for the periods presented have been included. Operating results for the three and nine-months ended December 31, 2021 are not necessarily indicative of the results that may be expected for the year ending March 31, 2022, for any other interim period, or for any other future year.

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 unaudited condensed 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 unaudited condensed 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.

There have been no significant changes in the Company's accounting policies from those disclosed in its Annual Report.

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 and accompanying notes 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 and accompanying notes 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 nine months ended December 31, 2021 and the fiscal year ended March 31, 2021, the Company incurred net losses of \$58.6 million and \$32.4 million, respectively. As of December 31, 2021, the Company's cash and cash equivalents totaled \$81.9 million and its accumulated deficit was \$849.6 million. As a result of the Company's decision to terminate its license agreement with Oxford Biomedica (UK) Ltd. ("Oxford") to develop and commercialize AXO-Lenti-PD gene therapy for the treatment of Parkinson's disease (the "Oxford Agreement") that is expected to become effective by March 31, 2022 (see Note 3(B) and Note 10), the Company estimates that its current cash and cash equivalents are sufficient to support operations into the second half of calendar year 2023, including beyond the expected dates of major upcoming milestones for the Company's AXO-AAV-GM1 and AXO-AAV-GM2 gene therapy programs. 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 unaudited condensed 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 December 31, 2021 and through the date of issuance of these unaudited condensed consolidated financial statements and accompanying notes. 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) Net Loss per Share of Common Stock:

Basic net loss per share of common stock is computed by dividing the net loss applicable to holders of common stock by the weighted-average number of shares of common stock and 3,301,998 pre-funded warrants (see Note 7(B)) outstanding during the period, without further consideration for potentially dilutive securities. The pre-funded warrants were fully exercised in July 2021 (see Note 7(B)). In accordance with ASC Topic 260, *Earnings Per Share*, the pre-funded warrants were included in the computation of basic net loss per share because the exercise price was negligible and they were 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 holders 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 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. Restricted Stock Units ("RSUs") and stock options outstanding for totals of 5.1 million and 3.2 million shares of common stock were not included in the calculation of diluted weighted-average shares of common stock outstanding for the three and nine-months ended December 31, 2021 and December 31, 2020, respectively, because they were anti-dilutive given the net loss of the Company.

(E) 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 and 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, and restricted cash consists of interest-bearing deposits denominated in the U.S. dollar. Cash and restricted cash are stated at their historical carrying amounts, which approximate fair value due to their short-term nature. The carrying values of the Company's money market fund included in cash and cash equivalents of \$77.0 million and \$114.0 million at December 31, 2021 and March 31, 2021, respectively, approximated their fair values, which are 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 December 31, 2021 and March 31, 2021 in determining such values (in thousands):

	As of December 31, 2021				As of March 31, 2021			
	Fair Value	Price Quotations (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Fair Value	Price Quotations (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market fund	\$ 77,000	\$ 77,000	\$ —	\$ —	\$ 114,000	\$ 114,000	\$ —	\$ —

(F) Recent Accounting Pronouncements:

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 accompanying notes because it does not currently have any investments or trade receivables outstanding, the impact on the Company's consolidated financial statements and accompanying notes 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.

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. During the three and nine-months ended December 31, 2021, the Company incurred totals of \$9.0 million and \$19.3 million, respectively, of program-specific costs related to its AXO-AAV-GM1 and AXO-AAV-GM2 programs within research and development expenses in its unaudited condensed consolidated statements of operations, including a total of \$3.0 million for license fee milestones due under the terms of the UMMS Agreement, and \$1.8 million and \$2.6 million during the three and nine-months ended December 31, 2020, respectively. The Company paid UMMS totals of \$3.0 million and \$4.9 million during the three and nine-months ended December 31, 2021, respectively, and \$13 thousand and \$25 thousand during the three and nine-months ended December 31, 2020, respectively.

(B) Oxford Biomedica License Agreement:

In June 2018, the Company entered into the Oxford Agreement with 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. In February 2022, the Company provided notice of termination to Oxford of the Oxford Agreement, which termination is expected to become effective by March 31, 2022 (see Note 10). The Company incurred \$8.3 million and \$9.3 million of AXO-Lenti-PD program-specific costs within research and development expenses in its unaudited condensed consolidated statement of operations during the three and nine-months ended December 31, 2021, respectively, including a \$2.0 million nonrecurring development milestone achieved, and \$1.4 million and \$4.8 million during the three and nine-months ended December 31, 2020, respectively. The Company paid Oxford totals of \$0.6 million and \$0.6 million during the three and nine-months ended December 31, 2021, respectively, and \$1.4 million and \$2.5 million during the three and nine-months ended December 31, 2020, respectively.

Note 4—Investment in Arvelle Therapeutics B.V.

In February 2021, the Company sold its investment of 8.1 million shares of nonredeemable preferred stock (the "Arvelle Shares") of Arvelle Therapeutics B.V. ("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 and that is recorded as restricted cash in the Company's unaudited condensed consolidated balance sheet at December 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 originally purchased its Arvelle Shares in February 2019 and May 2020 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 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 that was collected during the three months ended June 30, 2021.

Note 5—Accrued Expenses

As of December 31, 2021, and March 31, 2021, accrued expenses consisted of the following (in thousands):

	December 31, 2021	March 31, 2021
Research and development expenses	\$ 4,739	\$ 6,091
Bonuses and other compensation expenses	2,323	2,331
Other expenses	700	774
Total accrued expenses	<u>\$ 7,762</u>	<u>\$ 9,196</u>

Note 6—Long-term Debt

In April 2020, the Company fully prepaid \$15.7 million of outstanding principal, together with \$0.3 million of accrued interest, fees and other amounts, due under its loan and security agreement (the "Loan Agreement") with Hercules Capital, Inc. ("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 three months ended June 30, 2020. 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 7—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 (see Note 1).

(B) Transactions:

In February 2020, as part of a follow-on public offering, the Company issued and sold pre-funded warrants to purchase up to 3,301,998 shares of common stock at an offering price of \$3.74999 and an exercise price of \$0.00001 per pre-funded warrant, which were fully exercised in July 2021. The pre-funded warrants were classified as equity and the fair value of the pre-funded warrants was recorded as a credit to additional paid-in capital and was not subject to remeasurement.

The Company has 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. During the nine months ended December 31, 2020, which was the inception of this program, the Company sold approximately 17.0 million shares of its common stock for total proceeds of approximately \$53.2 million, net of brokerage fees. During the nine months ended December 31, 2021, the Company sold approximately 0.7 million shares of its common stock for total proceeds of approximately \$1.6 million, net of brokerage fees, under this program. As of December 31, 2021, the Company sold a total of approximately 30.4 million shares of its common stock for aggregate proceeds of approximately \$92.0 million, net of brokerage fees, under and since the inception of this program.

Note 8—Stock-Based Compensation**(A) Amended and Restated 2015 Equity Incentive Plan:**

In March 2015, the Company adopted its 2015 Equity Incentive Plan, which was (i) amended and restated in June 2017 by its Board of Directors and became effective upon stockholder approval in August 2017, (ii) further amended and restated in October 2020 by its Board of Directors, and (iii) further amended and restated in August 2021 by its Board of Directors and became effective upon stockholder approval in September 2021 (the "2015 Plan"). In April 2021 and April 2020, the number of shares of common stock authorized for issuance under the 2015 Plan increased automatically by 2.8 million and 1.6 million, respectively, in accordance with the terms of the 2015 Plan. Upon amendment and restatement by the Company's board of directors and stockholder approval of the 2015 Plan in August 2021 and September 2021, respectively, the number of shares of common stock authorized for issuance under the 2015 Plan increased by 5.0 million. At December 31, 2021, totals of 13.4 million shares of common stock were authorized for issuance and 7.6 million shares of common stock were available for future issuance under the 2015 Plan.

(B) Stock Options:

Time-based stock options granted to the Company's employees vest over a period of either (i) 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 equal quarterly installments thereafter for such stock options granted prior to April 2021, or (ii) three years with one-third of the shares of common stock underlying the stock option vesting on the first anniversary of the vesting commencement date and the remainder vesting in 8 equal quarterly installments thereafter for such stock options granted since April 2021, each 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. Options with market-based performance conditions vest based on the trading price for the Company's shares of common stock exceeding certain closing price thresholds.

Stock options granted under the 2015 Plan provide option holders, if provided for by the terms of the option agreement or 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.

During the nine months ended December 31, 2021 and 2020, the Company granted options to purchase totals of 1.6 million shares and 0.4 million shares, respectively, of its common stock under the 2015 Plan, with weighted-average exercise prices of \$2.47 and \$3.72, respectively, and estimated aggregate grant date fair values of \$3.3 million and \$1.3 million, respectively. There were no options with market-based performance conditions granted under the 2015 Plan during the nine months ended December 31, 2021 and 2020. At December 31, 2021, options to purchase a total of 3.1 million shares of common stock were outstanding under the 2015 Plan with a weighted-average exercise price of \$8.04 per share, including options with market-based performance conditions to purchase 0.3 million shares of common stock at a weighted-average exercise price of \$8.01 per share. At December 31, 2021, vested options to purchase a total of 1.1 million shares of common stock were outstanding under the 2015 Plan, with no options with market-based performance conditions vested and outstanding. During the nine months ended December 31, 2021 and 2020, the aggregate grant date fair values of stock options that vested under the 2015 Plan were \$2.0 million and \$3.0 million, respectively.

(C) Restricted Stock Units:

RSUs granted during the nine months ended December 31, 2021 and December 31, 2020 vest in three equal annual installments commencing on the first anniversary of the vesting commencement date, subject to continuing service. 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. During the nine months ended December 31, 2021 and December 31, 2020, the Company granted RSUs for totals of 1.5 million and 1.1 million shares, respectively, of its common stock to its employees under the 2015 Plan, with aggregate grant date fair values of \$3.6 million and \$3.8 million, respectively. At December 31, 2021, RSUs for approximately 1.9 million shares of common stock were outstanding, of which none were vested. During the nine months ended December 31, 2021 and December 31, 2020, the total grant date fair values of RSUs that vested under the 2015 Plan were \$1.0 million and \$1.0 million, respectively.

(D) Stock-based Compensation Expense:

The Company recorded total stock-based compensation expense of \$1.0 million and \$3.7 million for the three and nine-months ended December 31, 2021, respectively, and \$0.8 million and \$3.5 million for the three and nine-months ended December 31, 2020, respectively, related to options and RSUs granted to its employees and directors, excluding stock-based compensation expense allocated to the Company from its affiliate, Roivant Sciences Ltd. ("RSL") (see Note 8(E)). This stock-based compensation expense was included in research and development and general and administrative expenses in the Company's unaudited condensed consolidated statements of operations. At December 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 \$7.6 million, which is expected to be recognized over a remaining weighted-average service period of 2.0 years.

(E) RSL Equity Instruments:

Certain employees of the Company were granted RSL equity instruments for which the Company recognized stock-based compensation expense of \$0.4 million and \$6.3 million during the three and nine-months ended December 31, 2021, respectively, and which is recorded to general and administrative expenses in the Company's unaudited condensed consolidated statements of operations. Certain of these RSL equity instruments were granted to the Company's former CEO (the "RSL Equity Instruments"), who resigned as the Company's CEO in January 2022. The RSL Equity Instruments vest based on the satisfaction of time-based service and liquidity event requirements. The liquidity event vesting requirement was determined to be met upon the closing of RSL's business combination with Montes Archimedes Acquisition Corp., a special purpose acquisition company, on September 30, 2021. Accordingly, the Company commenced recognition of stock-based compensation expense for the RSL Equity Instruments on September 30, 2021.

Note 9—Commitments and Contingencies

As of December 31, 2021, the Company had entered into commitments under the UMMS Agreement (see Note 3(A)); the Oxford Agreement (see Note 3(B)) for which the Company provided notice of termination to Oxford of the Oxford Agreement in February 2022, which termination is expected to become effective by March 31, 2022 (see Note 10); services agreements with certain of RSL's wholly owned subsidiaries; and agreements to rent office and research and development laboratory spaces. 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- to 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 had 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.

Note 10—Subsequent Events

In February 2022, the Company provided notice of termination to Oxford of the Oxford Agreement, which termination is expected to become effective by March 31, 2022 (see Notes 2, 3(B) and 9).

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition, results of operations and cash flows should be read in conjunction with (i) the interim unaudited condensed consolidated financial statements and the related notes thereto included elsewhere in this Quarterly Report on Form 10-Q, and (ii) the audited consolidated financial statements and notes thereto and management's discussion and analysis of financial condition and results of operations for the fiscal year ended March 31, 2021, included in our Annual Report on Form 10-K, filed with the Securities and Exchange Commission (the "SEC") on June 9, 2021.

This Quarterly Report on Form 10-Q 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 Quarterly Report on Form 10-Q 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 II, Item 1A of this Quarterly Report on Form 10-Q and in our other filings with the 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.

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 two clinical-stage programs: (i) the AXO-AAV-GM1 program for the treatment of GM1 gangliosidosis in which we have completed the targeted enrollment and dosing of five patients in the late-infantile/juvenile (Type II) low-dose cohort of Stage 1 and three late-infantile/juvenile (Type II) patients in the higher-dose cohort of the study, and we continue to collect information from additional Type II patients for potential enrollment in Stage 2 of the trial. Screening of Type I (infantile-onset) patients for the low- and high-dose cohorts has been initiated and we have dosed two early infantile (Type I) patients - one in August 2021 and the other in September 2021; and (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 investigational new drug ("IND") from the FDA in November 2020, and in which we dosed the first four infantile and juvenile patients in January 2021, May 2021, September 2021 and November 2021. We expect continued patient identification, screening, and enrollment in the mid-dose cohort in Stage 1 of the dose-ranging trial throughout 2022.

We are dedicated to realizing the potential of gene therapies to offer transformative patient outcomes in areas of high unmet medical need. 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.

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, including within the United States, 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, certain elderly patients in previous clinical trials were either unable to, or refused to, participate in clinical assessments at our research sites in the United Kingdom due to the COVID-19 pandemic. 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, including as variant strains of the virus emerge, 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 new outbreaks or emerging variant strains of the virus, 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. While vaccines have become available in many countries and most economies have reopened, 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. New waves of outbreak or variant strains of the virus have emerged and may result in re-closures or other preventative measures. 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 II, Item 1A in this Quarterly Report on Form 10-Q.

Key Business Updates

AXO-AAV-GM1 and AXO-AAV-GM2 Programs (Including Tay-Sachs and Sandhoff diseases)

AXO-AAV-GM1

We presented updated safety data for our AXO-AAV-GM1 gene therapy program at the 18th Annual WORLDSymposium™ 2022, held from February 7 to February 11, 2022. Ten patients across all pediatric subtypes (early infantile, late infantile, and juvenile) of GM1 gangliosidosis have received AXO-AAV-GM1 gene therapy to-date. AXO-AAV-GM1 remains generally well tolerated in all ten patients at both the low and high doses to-date. There have been no reported drug-related serious adverse events, the majority of adverse events were considered mild to moderate and no safety signals have been identified.

The totality of the data have demonstrated a favorable risk: benefit profile and a dose-dependent improvement in key biomarkers of disease activity (β -galactosidase enzyme activity in the serum and GM1 ganglioside activity in the cerebrospinal fluid) across the low and high-dose cohorts.

Based on developmental and mobility assessments, there was no clinical evidence of disease progression in 4 of 5 low-dose subjects at 12 months or in the high-dose cohort at 6 months.

We expect to present a data update from Stage 1 of the Phase 1/2 study, including a first look at Type I (early-infantile) patients treated in the low-dose cohort and longer-term data from the Type II (late-infantile to juvenile) patient cohort at future scientific conferences in the first half of calendar year 2022, and we intend to engage with the FDA to review Stage 1 data and discuss next steps for clinical development in calendar year 2022.

AXO-AAV-GM2

We have dosed the first four patients in our open-label, two-stage Phase 1/2 clinical trial investigating AXO-AAV-GM2 in Tay-Sachs and Sandhoff diseases under an IND in January 2021, May 2021, September 2021 and November 2021, including one patient at the starting dose and three patients at the low dose. We expect continued patient identification, screening, and enrollment in the mid-dose cohort (n= ~3) in Stage 1 of the dose-ranging trial throughout calendar year 2022.

AXO-Lenti-PD Program

SUNRISE-PD Phase 1/2 Clinical Trial of AXO-Lenti-PD

Three GMP batches successfully completed fill and finish, achieving target titers using an updated suspension-based manufacturing process. All three GMP batches received GMP certification by a Qualified Person in the fourth calendar quarter of 2021. After a thorough analysis of the Parkinson's landscape, in February 2022, we provided notice of termination to Oxford Biomedica (UK) Ltd. ("Oxford") of the license agreement for the development and commercialization of AXO-Lenti-PD with Oxford due to several factors, including resource requirements and development timelines to reach meaningful value inflection for the program and an increasingly challenging market and regulatory environment for Parkinson's disease. The termination of the AXO-Lenti-PD program is expected to significantly extend our cash runway and allow us to focus our development efforts on our other clinical programs, which termination is expected to become effective by March 31, 2022.

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 Expenses

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 the University of Massachusetts Medical School ("UMMS") and Oxford.

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 recruiting expenses, for research and development personnel; and
- other expenses, which include research and development software costs, travel expenses, laboratory facility rental costs and research and development equipment depreciation expenses, as well as 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 partner, UMMS. We expect that our quarterly research and development expenses through the fiscal year ending March 31, 2023 will decline significantly relative to those incurred during the three months ended December 31, 2021, as a result of our decision to terminate the AXO-Lenti-PD gene therapy program for the treatment of Parkinson's disease that is expected to become effective by March 31, 2022, while we continue the enrollment of patients in our GM1 and GM2 clinical trials and commission the manufacturing of clinical supplies for our GM1 and GM2 clinical trials.

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 Expenses

General and administrative expenses consist primarily of employee-related expenses such as salaries, benefits and travel expenses for our general and administrative personnel; stock-based compensation, including stock-based compensation allocated to us from our affiliate, Roivant Sciences Ltd. ("RSL"), for certain RSL equity instruments granted to certain of our employees (primarily our former CEO (the "RSL Equity Instruments"), who resigned as our CEO in January 2022); non-employee benefit insurance premiums; third-party legal and accounting fees; information technology costs; office rent, fixed asset depreciation and other overhead costs; and consulting services. In the near term, we anticipate that:

- excluding stock-based compensation expense, our general and administrative expenses will at least approximate those incurred during the three and nine-months ended December 31, 2021; and

- our general and administrative stock-based compensation expense will decline significantly relative to that incurred during the nine months ended December 31, 2021, which included \$6.3 million of stock-based compensation expense associated with the RSL Equity Instruments, for which expensing commenced upon the liquidity event vesting condition being met upon the closing of RSL's business combination with Montes Archimedes Acquisition Corp. ("MAAC") on September 30, 2021. During the three months ended December 31, 2021, our general and administrative expenses included \$0.4 million of such stock-based compensation expense associated with the RSL Equity Instruments.

Results of Operations for the Three and Nine-Months Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the three and nine-months ended December 31, 2021 and 2020 (in thousands):

	Three Months Ended December 31,			Nine Months Ended December 31,		
	2021	2020	Change	2021	2020	Change
Operating expenses:						
Research and development expenses						
(includes stock-based compensation expense of \$130 and \$259 for the three months ended December 31, 2021 and 2020, respectively, and \$1,051 and \$1,280 for the nine months ended December 31, 2021 and 2020, respectively)	\$ 21,287	\$ 6,407	\$ 14,880	\$ 40,793	\$ 16,659	\$ 24,134
General and administrative expenses						
(includes stock-based compensation expense of \$1,268 and \$617 for the three months ended December 31, 2021 and 2020, respectively, and \$8,966 and \$2,294 for the nine months ended December 31, 2021 and 2020, respectively)	4,086	4,198	(112)	17,693	13,329	4,364
Total operating expenses	25,373	10,605	14,768	58,486	29,988	28,498
Interest expense	7	1	6	19	798	(779)
Other expense (income)	76	98	(22)	86	(1,388)	1,474
Loss before income tax benefit	(25,456)	(10,704)	(14,752)	(58,591)	(29,398)	(29,193)
Income tax benefit	—	(188)	188	(28)	(304)	276
Net loss	\$ (25,456)	\$ (10,516)	\$ (14,940)	\$ (58,563)	\$ (29,094)	\$ (29,469)

Research and Development Expenses

Our research and development expenses during the three and nine-months ended December 31, 2021 and 2020 consisted of the following (in thousands):

	Three Months Ended December 31,			Nine Months Ended December 31,		
	2021	2020	Change	2021	2020	Change
Program-specific costs:						
AXO-AAV-GM1	\$ 4,702	\$ 1,391	\$ 3,311	\$ 11,796	\$ 2,466	\$ 9,330
AXO-AAV-GM2	4,297	455	3,842	7,527	180	7,347
AXO-Lenti-PD	8,263	1,387	6,876	9,296	4,774	4,522
Unallocated internal costs:						
Personnel-related	2,464	1,627	837	7,127	5,267	1,860
Stock-based compensation expense	130	259	(129)	1,051	1,280	(229)
Other	1,431	1,288	143	3,996	2,692	1,304
Total research and development expenses	\$ 21,287	\$ 6,407	\$ 14,880	\$ 40,793	\$ 16,659	\$ 24,134

Research and development expenses were \$21.3 million for the three months ended December 31, 2021 and \$6.4 million for the three months ended December 31, 2020, increasing by \$14.9 million. The \$14.9 million increase was primarily related to:

- (i) increased AXO-AAV-GM1 program expenses primarily related to clinical trial material manufacturing expenses for the planned enrollment of infantile patients in the high-dose cohort, as well as a \$1.5 million license fee milestone due in December 2021 under the terms of our exclusive license agreement with UMMS (the "UMMS Agreement");
- (ii) increased AXO-AAV-GM2 program expenses primarily related to a \$1.5 million license fee milestone due in December 2021 under the terms of the UMMS Agreement, as well as non-GMP and GMP manufacturing expenses;
- (iii) increased AXO-Lenti-PD program expenses, primarily related to clinical trial material manufacturing expenses resulting from Qualified Person certification of GMP batches and a \$2.0 million nonrecurring development milestone achieved upon the successful completion of the updated suspension-based manufacturing process for the AXO-Lenti-PD program in the fourth calendar quarter of 2021; and
- (iv) increased personnel-related costs primarily due to increased headcount.

Research and development expenses were \$40.8 million for the nine months ended December 31, 2021 and \$16.7 million for the nine months ended December 31, 2020, increasing by \$24.1 million. The \$24.1 million increase was primarily related to:

- (i) increased AXO-AAV-GM1 program expenses primarily related to clinical trial material manufacturing expenses for the planned enrollment of infantile patients in the high-dose cohort, as well as a \$1.5 million license fee milestone due in December 2021 under the terms of the UMMS Agreement;
- (ii) increased AXO-AAV-GM2 program expenses primarily related to non-GMP and GMP manufacturing expenses, clinical trial expenses associated with the ongoing enrollment of patients in the low-dose cohort and for the planned enrollment of patients in the mid-dose cohort, as well as a \$1.5 million license fee milestone due in December 2021 under the terms of the UMMS Agreement;
- (iii) increased AXO-Lenti-PD program expenses, primarily related to clinical trial material manufacturing expenses resulting from Qualified Person certification of GMP batches and a \$2.0 million nonrecurring development milestone achieved upon the successful completion of the updated suspension-based manufacturing process for the AXO-Lenti-PD program in the fourth calendar quarter of 2021, which were partially offset by decreased analytical development costs; and
- (iv) increased personnel-related costs primarily due to increased headcount.

General and Administrative Expenses

General and administrative expenses were \$4.1 million for the three months ended December 31, 2021 and \$4.2 million for the three months ended December 31, 2020. The decrease of \$0.1 million was primarily related to decreases totaling \$1.0 million for (i) rent, depreciation and overhead expenses due to the downsizing of our New York office footprint, and (ii) tax, legal, auditing and accounting fees resulting primarily from the simplification of our corporate structure and the domestication of Sio Gene Therapies Inc. from Bermuda to Delaware that was completed in November 2020. These decreases were partially offset by an increase of \$0.7 million of stock-based compensation expense primarily associated with the RSL Equity Instruments, for which expensing commenced upon the liquidity event vesting condition being met upon the closing of RSL's business combination with MAAC on September 30, 2021.

General and administrative expenses were \$17.7 million for the nine months ended December 31, 2021 and \$13.3 million for the nine months ended December 31, 2020. The increase of \$4.4 million was primarily related to \$6.7 million of stock-based compensation expense primarily associated with the RSL Equity Instruments recorded during the nine months ended December 31, 2021. This increase was partially offset by decreases totaling \$2.7 million for (i) rent, depreciation and overhead expenses due to the downsizing of our New York office footprint, and (ii) tax, legal, auditing and accounting fees resulting primarily from the simplification of our corporate structure and the domestication of Sio Gene Therapies Inc. from Bermuda to Delaware that was completed in November 2020.

Interest Expense

Interest expense was \$7 thousand and \$19 thousand for the three and nine-months ended December 31, 2021, and \$1 thousand and \$0.8 million for the three and nine-months ended December 31, 2020. The decrease in interest expense during the nine months ended December 31, 2021 compared to the prior year period was due to the April 2020 prepayment in full of the \$15.7 million outstanding principal balance on our loan and security agreement with Hercules Capital, Inc. ("Hercules").

Other Expense (Income)

Other expense was \$76 thousand and \$98 thousand for the three months ended December 31, 2021 and 2020, respectively, and consisted primarily of foreign exchange losses.

Other expense (income) was \$86 thousand and \$(1.4) million for the nine months ended December 31, 2021 and 2020, respectively. Other expense for the nine months ended December 31, 2021 consisted primarily of foreign exchange losses. Other income for the nine months ended December 31, 2020 consisted primarily of a gain of approximately \$2.2 million associated with the exercise of a right to purchase convertible preferred stock in Arvelle Therapeutics B.V. ("Arvelle") that was sold in February 2021, which was partially offset by foreign exchange losses.

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 December 31, 2021, we had \$81.9 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 December 2023.

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. 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 European Medicines Agency 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;
- 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 nine months ended December 31, 2021 and the fiscal year ended March 31, 2021, we incurred net losses of \$58.6 million and \$32.4 million, respectively. As of December 31, 2021, our cash and cash equivalents totaled \$81.9 million and our accumulated deficit was \$849.6 million. As a result of our decision to terminate the AXO-Lenti-PD gene therapy program for the treatment of Parkinson's disease that is expected to become effective by March 31, 2022, we estimate that our current cash and cash equivalents are sufficient to support operations into the second half of calendar year 2023, including beyond the expected dates of major upcoming milestones for our AXO-AAV-GM1 and AXO-AAV-GM2 gene therapy programs. 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 unaudited condensed consolidated financial statements and footnotes 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 has been, and may continue to be, adversely impacted by, among other things, 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. During the nine months ended December 31, 2020, which was the inception of this program, we sold approximately 17.0 million shares of our common stock for total proceeds of approximately \$53.2 million, net of brokerage fees, under this program. During the nine months ended December 31, 2021, we sold approximately 0.7 million shares of our common stock for total proceeds of approximately \$1.6 million, net of brokerage fees, under this program. As of December 31, 2021, we sold a total of approximately 30.4 million shares of our common stock for aggregate proceeds of approximately \$92.0 million, net of brokerage fees, under and since the inception of this program.

Cash Flows

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

	Nine Months Ended December 31,	
	2021	2020
Net cash used in operating activities	\$ (42,524)	\$ (36,348)
Net cash provided by (used in) investing activities	4,007	(247)
Net cash provided by financing activities	1,441	36,862

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 nine months ended December 31, 2021, net cash used in operating activities was \$42.5 million and was primarily attributable to a net loss of \$58.6 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 a decrease of \$1.4 million in accrued expenses, which were partially offset by \$10.0 million of non-cash stock-based compensation expense, an increase in accounts payable of \$5.3 million and a decrease in prepaid expenses and other current assets of \$2.1 million.

For the nine months ended December 31, 2020, net cash used in operating activities was \$36.3 million and was primarily attributable to a net loss of \$29.1 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 net decreases in accrued expenses of \$3.6 million and accounts payable of \$3.4 million, an increase in prepaid expenses and other current assets of \$3.3 million, and a gain of \$2.2 million associated with the exercise of a right to purchase convertible preferred stock in Arvelle that was sold in February 2021, which were partially offset by \$3.6 million of non-cash stock-based compensation expense.

Investing Activities

Net cash provided by investing activities was \$4.0 million for the nine months ended December 31, 2021 and consisted primarily of \$4.3 million of cash proceeds from the sale of our long-term investment in Arvelle, partially offset by purchases of fixed assets. Net cash used in investing activities was \$0.2 million for the nine months ended December 31, 2020 and related to purchases of fixed assets.

Financing Activities

For the nine months ended December 31, 2021, net cash provided by financing activities was approximately \$1.4 million and consisted of net proceeds from the issuance and sale of our shares of common stock under our share sales agreement with SVB Leerink LLC. For the nine months ended December 31, 2020, net cash provided by financing activities was approximately \$36.9 million and consisted primarily of \$52.5 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.

Contractual Obligations

Our contractual obligations did not materially change during the nine months ended December 31, 2021 as compared to those disclosed in our Annual Report on Form 10-K for the year ended March 31, 2021.

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.

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 unaudited condensed consolidated financial statements and accompanying notes, which have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP"). The preparation of these unaudited condensed 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 unaudited condensed consolidated financial statements in this Quarterly Report on Form 10-Q and in Note 2, "Summary of Significant Accounting Policies," to our audited consolidated financial statements in our 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 accompanying notes and consider these to be our critical accounting policies and estimates and are "critical accounting estimates." There have been no material changes to our critical accounting policies and significant judgments and estimates as compared to the critical accounting policies and significant judgments and estimates described in our Annual Report.

Recent Accounting Pronouncements

For a discussion of recent accounting pronouncements, see "Note 2(F)—Recent Accounting Pronouncements" in the accompanying notes to the unaudited condensed consolidated financial statements included in "Item 1—Financial Statements" of this Quarterly Report on Form 10-Q for additional information.

Item 3. 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 December 31, 2021, we had total cash and cash equivalents and restricted cash of \$83.1 million, with cash consisting of non-interest-bearing deposits denominated in the U.S. dollar, Swiss franc and Euro, 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, and restricted cash consisting of interest-bearing deposits denominated in the U.S. dollar. 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 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Under the supervision of our principal executive and financial officer, we evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021, the end of the period covered by this Quarterly Report on Form 10-Q. 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 and financial officer, as appropriate, to allow for timely decisions regarding required disclosure. Based on this evaluation, our principal executive and financial officer concluded that our disclosure controls and procedures were effective as of December 31, 2021, at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(d) and 15d-15(d) under the Exchange Act) that occurred during the period covered by this Quarterly Report on Form 10-Q that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Our management, including our principal executive and 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.

PART II: OTHER INFORMATION

Item 1. 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 an adverse effect on our business, operating results or financial condition.

Item 1A. Risk Factors

You should carefully consider the following risk factors, in addition to the other information contained in this Quarterly Report on Form 10-Q, including the section of this report titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our unaudited condensed 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 common stock could decline. This Quarterly Report on Form 10-Q 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. You should not interpret our disclosure of any of the following risks to imply that such risks have not already materialized.

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. Our gene therapy-focused 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. 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.

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 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") 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 and operations, 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. 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, including emerging variant strains of the virus. 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, 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, certain elderly patients in previous clinical trials were either unable to, or refused to, participate in clinical assessments at our research sites in the United Kingdom due to the COVID-19 pandemic. 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. While vaccines have become available in many countries and most economies have reopened, 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. New waves of outbreak or variant strains of the virus have emerged and may result in re-closures or other preventative measures. 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.

In order to meet our long-term operating requirements, we will need, among other things, additional capital resources. We could use our available capital resources sooner than we currently expect. 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 has been, and may continue to be, adversely impacted by, among other things, 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 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. In addition, we expect to prioritize certain of our clinical programs over others depending on our capital resources and our access to additional capital sources. For example, in February 2022, we provided notice of termination to Oxford Biomedica (UK) Ltd. ("Oxford") of the license agreement for the development and commercialization of AXO-Lenti-PD with Oxford (the "Oxford Agreement") in order to significantly extend our cash runway and focus our development efforts on our other clinical programs, which termination is expected to become effective by March 31, 2022. As a result, we will be heavily dependent on the success of our remaining gene therapy programs. 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 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 our product candidates in development, including GM1 gangliosidosis or GM2 gangliosidosis (including Tay-Sachs and Sandhoff diseases), 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.

If we are unable to successfully develop and commercialize any of our remaining product candidates, our business will be harmed.

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. We anticipate that our current cash and cash equivalents are sufficient to fund our operations beyond the expected dates of major upcoming milestones for our AXO-AAV-GM1 and AXO-AAV-GM2 gene therapy programs. However, 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 for any of our clinical programs. 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 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;
- 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 nine months ended December 31, 2021 and the fiscal year ended March 31, 2021, we incurred net losses of \$58.6 million and \$32.4 million, respectively. As of December 31, 2021, our cash and cash equivalents totaled \$81.9 million and our accumulated deficit was \$849.6 million.

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 continue to make significant payments to third parties under the agreements pursuant to which we acquired our gene therapy product candidates.

Under our agreement with the University of Massachusetts Medical School ("UMMS"), 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.

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, capital resource allocation or any other reason, and may terminate the related license. For example, in June 2019, we decided to terminate an agreement with Benitec Biopharma Limited following our decision to no longer pursue development of AXO-AAV-OPMD and related gene therapy product candidates. In addition, in February 2022, we provided notice of termination to Oxford of the Oxford Agreement for the development and commercialization of AXO-Lenti-PD and related gene therapy product candidates, which termination is expected to become effective by March 31, 2022. Changes or reductions in development efforts or activities by us for any of our in-licensed clinical programs may also negatively impact our relationships with our license counterparties or result in the early termination of such programs.

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. For example, our Chief Research and Development Officer recently resigned from his position, and in January 2022, our Chief Executive Officer resigned. If we lose additional 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 (EU) 2016 /679 ("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.

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.

We are subject to stringent U.S. and foreign privacy laws, regulations and standards related to data privacy and security. If we fail to comply with such requirements, we may be subject to liabilities that adversely affect our business, operations and financial performance, disruption to our clinical trials or the commercialization of our products, and/or harm to our reputation.

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, in the U.S., 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 (including health-related personal data) across the European Economic Area ("EEA"). Also, notwithstanding the U.K.'s withdrawal from the EU, the data protection obligations of the GDPR continue to apply to U.K.-related processing of personal data in substantially unvaried form under the so-called "U.K. GDPR" (the GDPR as it continues to form part of law in the U.K.). Accordingly, references in this section to the GDPR are also deemed to be references to the U.K. GDPR in the context of the U.K., unless the context requires otherwise.

The GDPR has “extra-territorial” reach in that it applies to any processing of personal data that concerns the offering of goods or services to individuals in the EEA or U.K. (as applicable) and the monitoring of their behavior, regardless of the existence of an establishment in the EEA or U.K. (as applicable). As such, the GDPR applies to our clinical trials and other operations taking in place in the EEA and U.K.

The GDPR sets out a number of requirements that must be complied with when handling personal data, including: the obligation to appoint a data protection officer in certain circumstances; increased accountability and record-keeping obligations; increased transparency obligations for data controllers; onerous obligations on service providers who process personal data on our behalf; the obligation to carry out so-called data protection impact assessments in certain circumstances; obligations to comply with data subjects’ exercise of an increased set of rights in certain circumstances; a heightened and more codified standard of data subject consent; and the obligation to notify certain significant personal data breaches to the relevant supervisory authorities and affected individuals. In addition, the GDPR materially expands the definition of what is expressly provided to constitute personal data (including, for example, by clarifying that the GDPR applies to “pseudonymized” (key-coded) data, which is often processed by sponsors in the context of clinical trials where identification of underlying subjects is not required). As such, 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 (and/or in respect of the U.K. GDPR, 17.5 million pounds sterling) or up to 4% of annual global revenue (whichever is higher). 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. The GDPR also provides that member states may make their own national laws and regulations to introduce specific requirements related to the processing of “special categories of personal data”, which includes health-related personal data. In the U.K., the Data Protection Act 2018 complements the U.K. GDPR in this regard. This may lead to greater divergence in the application, interpretation and enforcement of the law that applies to the processing of personal data across the EEA and/or U.K., compliance with which, as and where applicable, may increase our costs and could increase our overall compliance risk. Such country-specific regulations could also limit our ability to collect, use and share data in the context of our EEA and/or U.K. operations, and/or could cause our compliance costs to increase, ultimately having an adverse impact on our business and harming our business and financial condition.

In addition, the GDPR prohibits the transfer of personal data from the EEA, U.K. and Switzerland to the U.S. and other countries in respect of which the European Commission or other relevant regulatory body has not issued a so-called “adequacy decision” (known as “third countries”), unless the parties to the transfer have implemented specific safeguards to protect the transferred personal data. One of the primary safeguards used for transfers of personal data to the U.S. was the EU-U.S. Privacy Shield framework administered by the U.S. Department of Commerce. However, certain recent EU court decisions cast doubt on the ability to use one of the primary alternatives to the EU-U.S. Privacy Shield and Swiss-U.S. Privacy Shield, namely the European Commission’s Standard Contractual Clauses, to lawfully transfer personal data to the U.S. and other third countries. In addition, the European Commission has recently published new versions of the Standard Contractual Clauses, which must be used for all new transfers of personal data from the EEA to third countries (including the United States) starting in September 2021, and all existing transfers of personal data from the EEA to third countries relying on the existing versions of the Standard Contractual Clauses must be replaced by December 2022. The implementation of the new Standard Contractual Clauses will necessitate significant contractual overhaul of our data transfer arrangements with customers, sub-processors and vendors. Use of both the existing and the new Standard Contractual Clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals, and additional supplementary technical, organizational and/or contractual measures and/or contractual provisions may need to be put in place.

At present, there are few if any viable alternatives to the Standard Contractual Clauses, and there remains some uncertainty with respect to the nature and efficacy of such supplementary measures in ensuring an adequate level of protection of personal data. As such, transfers of personal data from the EEA and the U.K. to the U.S. and other third countries may not fully comply with the cross-border data transfer restrictions set out in the GDPR. As supervisory authorities issue further guidance on personal data export mechanisms (including circumstances where the Standard Contractual Clauses can and cannot be used) and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines. In addition, if we are unable to transfer personal data between and among countries and regions in which we operate and/or engage providers and/or otherwise transfer personal data, this could affect the manner in which we receive and/or provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results and generally increase compliance risk as a result. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of operating our business.

Furthermore, following Brexit, the relationship between the U.K. and the EEA in relation to certain aspects of data protection law remains somewhat uncertain. In June 2021, the European Commission issued an adequacy decision under the GDPR which allows transfers (other than those carried out for the purposes of U.K. immigration control) of personal data from the EEA to the U.K. to continue without restriction for a period of four years. After that period, the adequacy decision may be renewed only if the U.K. continues to ensure an adequate level of data protection. During these four years, the European Commission will continue to monitor the legal situation in the U.K. and could intervene at any point if the U.K. deviates from the level of data protection in place at the time of issuance of the adequacy decision. If the adequacy decision is withdrawn or not renewed, transfers of personal data from the EEA to the U.K. will require a valid “transfer mechanism” and we may be required to implement new processes and put new agreements in place, such as Standard Contractual Clauses, to enable transfers of personal data from the EEA to the U.K. to continue, which could disrupt our operations.

In addition, while the U.K. data protection regime currently permits data transfers from the U.K. to the EEA and other third countries covered by a European Commission adequacy decision, and currently includes a framework to permit the continued use of the existing version of the Standard Contractual Clauses for personal data transfers from the U.K. to third countries, this is subject to change in the future, and any such changes could have implications for our transfers of personal data from the U.K. to the EEA and other third countries. In particular, the U.K. Information Commissioner’s Office has stated that it is working on its own bespoke version of the Standard Contractual Clauses and it is not clear whether the new Standard Contractual Clauses published by the European Commission will be accepted as a valid mechanism to permit the transfer of personal data from the U.K. to third countries and/or whether any U.K. version of the Standard Contractual Clauses will supersede the existing and/or new EU version of the Standard Contractual Clauses. This could necessitate the implementation of both U.K. and EU versions of Standard Contractual Clauses, which would require significant resources and result in significant cost to implement and manage.

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 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 predecessor, UMMS, 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 predecessor, UMMS, 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, any 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 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 for GM1 gangliosidosis to be LYS-GM101, a gene therapy product candidate being developed by Lysogene S.A., which initiated enrollment in a Phase 1/2 clinical trial in 2021, and PBGM01, a gene therapy program being developed by Passage Bio which received IND clearance and enrolled two patients in 2021. We consider our direct competitor for AXO-AAV-GM2 for GM2 gangliosidosis (including Tay-Sachs and Sandhoff disease) to be TSHA-101, a gene therapy product candidate being developed by Taysha Gene Therapies, which has an open clinical trial in Canada and initiated patient enrollment.

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 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 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 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 and GM2 gangliosidosis (including Tay-Sachs disease and Sandhoff 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. 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 a National Institutes of Health ("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 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 PHSAs 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), 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 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 inseparable 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 Trump 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 Trump 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, President Trump 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. 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.

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 agreement with UMMS, 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 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 and AXO-AAV-GM2, 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 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 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.

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 25.2% of our shares of common stock outstanding as of February 8, 2022, 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;

- 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 UMMS or comply with the terms of the worldwide exclusive license agreement to develop and commercialize gene therapy product candidates AXO-AAV-GM1 and AXO-AAV-GM2 with UMMS, or the termination of the Oxford 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 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 February 8, 2022, RSL beneficially owns approximately 25.2% 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. RSL recently entered into a business combination agreement with Montes Archimedes Acquisition Corp., a special purpose acquisition corporation, pursuant to which RSL has become a publicly-traded corporation. 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 February 8, 2022, 18,577,380 of our outstanding shares of common stock, representing 25.2% 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 \$35.1 million remaining available to be sold as of the issuance of the accompanying unaudited condensed consolidated financial statements and notes. 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 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 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 2. Unregistered Sales of Equity Securities and Use of Proceeds

None.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

On our Current Report on Form 8-K filed with the Securities and Exchange Commission on January 31, 2022, we announced the resignation of our Chief Executive Officer and director, Pavan Cheruvu, which became effective on January 31, 2022. We also announced the appointment of our Chief Financial and Accounting Officer and General Counsel, David Nassif, as Interim Chief Executive Officer and a director, effective on January 31, 2022. Dr. Cheruvu agreed to assist with the executive transition as a non-executive employee through February 15, 2022.

In connection with Mr. Nassif's appointment as Interim Chief Executive Officer, in addition to the compensation described in the Current Report on Form 8-K, the Compensation Committee of our board of directors approved a grant of 546,500 restricted stock units for Mr. Nassif. One-third of the restricted stock units vest on February 8, 2023, February 8, 2024 and February 8, 2025, subject to Mr. Nassif providing continuous service to us through each such date.

The Compensation Committee of our board of directors has also agreed with Mr. Nassif to amend the severance terms in his employment agreement, dated November 4, 2019, to provide that:

- a. If Mr. Nassif's employment is terminated without cause or Mr. Nassif resigns for good reason on or within 12 months of a change in control, Mr. Nassif receives 2 times his base salary; and
- b. If a non-interim Chief Executive Officer is hired, Mr. Nassif's severance benefits revert back to the current benefits, which provide for 1.5 times his base salary in the event his employment is terminated without cause or he resigns for good reason on or within 12 months of a change in control, with certain exceptions in the event that a non-interim Chief Executive Officer is hired within three months of a change in control.

In addition, the Compensation Committee of our board of directors approved a 90-day consulting agreement for Dr. Cheruvu, to become effective as of February 15, 2022. Under the consulting agreement, Dr. Cheruvu will be paid \$1,000 per hour for his services subject to a 5-hour per month maximum. The terms of the agreement will not allow the continued vesting of any of Dr. Cheruvu's stock options or restricted stock units.

We intend to file copies of Mr. Nassif's amended and restated employment agreement and Dr. Cheruvu's consulting agreement as exhibits to our Annual Report on Form 10-K for the fiscal year ending March 31, 2022.

Item 6. Exhibits.

Exhibit Number	Description of Document	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
31.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1*#	Certification of Principal Executive Officer and 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 - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				
101.SCH*	XBRL Taxonomy Extension Schema Document.				
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.				
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document.				
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.				
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.				
104*	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibits 101).				

* Filed herewith.

These certifications are being furnished solely to accompany this Quarterly Report on Form 10-Q 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 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.

Date: February 11, 2022

By: /s/ David Nassif
Name: David Nassif
Title: Interim Chief Executive Officer; Chief Financial Officer; Chief Accounting Officer and General Counsel
(Principal Executive Officer, Principal Financial Officer and Principal Accounting Officer)

CERTIFICATION

I, David Nassif, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Sio Gene Therapies Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 11, 2022

By: /s/ David Nassif

David Nassif

Interim Chief Executive Officer; Chief Financial Officer; Chief Accounting Officer and General Counsel

(Principal Executive Officer, Principal Financial Officer and Principal Accounting Officer)

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

In connection with the Quarterly Report on Form 10-Q of Sio Gene Therapies Inc. (the "Company") for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, David Nassif, Principal Executive Officer and Principal Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 11, 2022

By: /s/ David Nassif

David Nassif

Interim Chief Executive Officer; Chief Financial Officer; Chief Accounting Officer and General Counsel

(Principal Executive Officer, Principal Financial Officer and Principal Accounting Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the SEC or its staff upon request.

This certification accompanies the Report, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), regardless of any general incorporation language contained in such filing.