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

FORM 10-Q

☒ **Quarterly Report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

For the quarterly period ended March 31, 2019
OR

☐ **Transition report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

For the transition period from _____ to _____.
Commission File Number: 001-37833

Audentes Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**46-1606174**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**

600 California Street, 17th Floor
San Francisco, California 94108
(Address of principal executive offices and zip code)

(415) 818-1001
(Registrant's telephone number, including area code)

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

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

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.:

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
Emerging growth company	☐		

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

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

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

Title of each class	**Trading Symbol**	**Name of exchange on which registered**
Common Stock, par value $0.00001 per share	**BOLD**	**The Nasdaq Global Market**

As of May 3, 2019, there were 44,290,458 shares of the Registrant's Common Stock, $0.00001 par value per share, outstanding.

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PART I

ITEM 1. CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

AUDENTES THERAPEUTICS, INC.
Condensed Consolidated Balance Sheets
(in thousands, except shares and per share amounts)

	March 31, 2019	December 31, 2018
Assets	*(Unaudited)*	
Current assets:		
Cash and cash equivalents	$ 133,160	$ 144,349
Short-term investments	236,344	269,958
Prepaid expenses and other current assets	3,651	5,465
Total current assets	373,155	419,772
Restricted cash - long-term	3,748	3,748
Long-term investments	5,517	—
Property and equipment, net	34,731	32,099
Right of use assets	21,089	—
Goodwill	3,631	3,631
Intangible assets	8,000	8,000
Other assets	5,305	5,305
Total assets	$ 455,176	$ 472,555
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 11,811	$ 8,123
Accrued liabilities	11,520	12,928
Operating lease liabilities	2,773	—
Contingent acquisition consideration payable	—	2,345
Deferred rent	—	456
Total current liabilities	26,104	23,852
Deferred rent - long-term	—	4,720
Asset retirement obligation - long-term	221	215
Operating lease liabilities - long-term	23,519	—
Contingent acquisition consideration payable - long-term	2,323	—
Deferred tax liability, net	1,014	1,014
Total liabilities	53,181	29,801
Stockholders' equity:		
Preferred stock, $0.00001 par value, 10,000,000 shares authorized as of March 31, 2019 and December 31, 2018; 0 shares issued and outstanding as of March 31, 2019 and December 31, 2018, respectively	—	—
Common stock, $0.00001 par value, 300,000,000 shares authorized as of March 31, 2019 and December 31, 2018; 43,760,677 and 43,546,786 shares issued and outstanding as of March 31, 2019 and December 31, 2018, respectively	—	—
Additional paid-in capital	770,789	762,284
Accumulated deficit	(368,861)	(319,470)
Accumulated other comprehensive income (loss)	67	(60)
Total stockholders' equity	401,995	442,754
Total liabilities and stockholders' equity	$ 455,176	$ 472,555

See accompanying notes to unaudited interim condensed consolidated financial statements.

AUDENTES THERAPEUTICS, INC.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except shares and per share amounts)

	Three Months Ended March 31,	
	2019	**2018**
Operating expenses:	*Unaudited*	
Research and development	$ 39,837	$ 19,891
General and administrative	11,993	6,519
Total operating expenses	51,830	26,410
Loss from operations	(51,830)	(26,410)
Interest income, net	2,472	859
Other expense, net	(33)	(20)
Net loss	(49,391)	(25,571)
Unrealized gains (losses) on investments, net	127	(14)
Comprehensive loss	$ (49,264)	$ (25,585)
Net loss per share, basic and diluted	$ (1.13)	$ (0.74)
Weighted-average number of shares used in computing net loss per share, basic and diluted	43,625,316	34,582,071

See accompanying notes to unaudited interim condensed consolidated financial statements.

AUDENTES THERAPEUTICS, INC.
Condensed Consolidated Statements of Stockholders' Equity
(in thousands, except shares and per share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount				
Balance, December 31, 2018	43,546,786	$ —	$ 762,284	$ (319,470)	$ (60)	$ 442,754
Exercise of stock options	213,891	—	3,005	—	—	3,005
Stock-based compensation expense	—	—	5,500	—	—	5,500
Net loss	—	—	—	(49,391)	—	(49,391)
Unrealized gain on investments, net	—	—	—	—	127	127
Balance, March 31, 2019	43,760,677	$ —	$ 770,789	$ (368,861)	$ 67	$ 401,995

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount				
Balance, December 31, 2017	29,901,368	$ —	$ 347,327	$ (190,649)	$ (80)	$ 156,598
Exercise of stock options	183,692	—	807	—	—	807
Stock-based compensation expense	—	—	3,385	—	—	3,385
Issuance of common stock, net of $14,201 in issuance costs	6,612,500	—	217,237	—	—	217,237
Net loss	—	—	—	(25,571)	—	(25,571)
Unrealized loss on investments, net	—	—	—	—	(14)	(14)
Balance, March 31, 2018	36,697,560	$ —	$ 568,756	$ (216,220)	$ (94)	$ 352,442

See accompanying notes to unaudited interim condensed consolidated financial statements.

AUDENTES THERAPEUTICS, INC.
Condensed Consolidated Statements of Cash Flows
(in thousands)

	Three Months Ended March 31,	
	2019	**2018**
Cash flows from operating activities:	*Unaudited*	
Net loss	$ (49,391)	$ (25,571)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,728	1,149
Amortization of right-of-use assets	580	—
Stock-based compensation	5,500	3,385
Accretion of discount on marketable securities	(1,090)	(121)
Change in fair value of contingent acquisition consideration payable	(22)	(2,284)
Other	6	34
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,814	275
Accounts payable	1,852	596
Accrued liabilities	(2,644)	(2,223)
Deferred rent	—	168
Operating lease liabilities	(553)	—
Net cash used in operating activities	(42,220)	(24,592)
Cash flows from investing activities:		
Purchases of property and equipment	(1,288)	(921)
Proceeds from maturities of marketable securities	146,802	34,775
Purchases of marketable securities	(117,488)	(35,294)
Net cash provided by (used in) investing activities	28,026	(1,440)
Cash flows from financing activities:		
Proceeds from exercise of stock options	3,005	807
Proceeds from issuance of common stock, net of issuance costs	—	217,122
Net cash provided by financing activities	3,005	217,929
Net (decrease) increase in cash, cash equivalents and restricted cash	(11,189)	191,897
Cash, cash equivalents and restricted cash at beginning of period	148,097	42,661
Cash, cash equivalents and restricted cash at end of period	$ 136,908	$ 234,558
Noncash investing and financing activities:		
Change in accounts payable and accrued liabilities related to property and equipment purchases	$ 3,072	$ 2,293
Deferred financing costs for follow-on offering	$ —	$ 115
Cash paid for amounts included in the measurement of lease liabilities:		
Cash used in operating activities:		
Operating leases	$ 1,323	$ —

See accompanying notes to unaudited interim condensed consolidated financial statements.

AUDENTES THERAPEUTICS, INC.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

1. Organization and Basis of Presentation

Audentes Therapeutics, Inc., or the Company, was incorporated in the State of Delaware on November 13, 2012. The Company is an AAV-based genetic medicines company focused on developing and commercializing innovative products for patients living with serious, rare neuromuscular diseases. The Company operates in one business segment, with its corporate headquarters located in San Francisco, California and its manufacturing and research operations located in South San Francisco, California.

The accompanying consolidated financial statements include the accounts of Audentes Therapeutics, Inc., and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Need for Additional Capital

The Company has incurred net losses from operations since inception and as of March 31, 2019, had an accumulated deficit of $368.9 million. The Company expects that its development activities will continue to generate operating losses over the next several years.

Liquidity

As of March 31, 2019, the Company had approximately $375.0 million of cash, cash equivalents and marketable securities, consisting of $133.2 million of cash and cash equivalents and $241.9 million of marketable securities. The Company believes that its balance of cash, cash equivalents and investments as of March 31, 2019 is sufficient to fund its current operational plan for at least the next twelve months, though it may pursue additional capital through the issuance of additional equity and potentially through strategic alliances with partner companies. If financing is not available at adequate levels or on acceptable terms, the Company may need to reevaluate its operating plans. In addition, if the Company's anticipated operating results are not achieved in future periods, planned expenditures may need to be reduced in order to extend the time period over which the then-available resources would be able to fund the Company's operations.

2. Summary of Significant Accounting Policies

The Company's significant accounting policies are detailed in Note 2 of the "Notes to Consolidated Financial Statements" in the Company's Annual Report on Form 10-K for the year ended December 31, 2018. Except as detailed below, there have been no material changes to the Company's significant accounting policies during the three months ended March 31, 2019, as compared to the significant accounting policies disclosed in Note 2 - *Significant Accounting Policies* included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018.

Leases

The Company determines if an arrangement is or contains a lease at inception by assessing whether the arrangement contains an identified asset and whether it has the right to control the identified asset. Right-of-use (ROU) assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. ROU assets and lease liabilities are recognized at the lease commencement date based on the present value of future lease payments over the lease term. As the implicit rate in the Company's leases is unknown, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of future lease payments. The Company gives consideration to its credit risk, term of the lease, total lease payments and adjust for the impacts of collateral, as necessary, when calculating its incremental borrowing rates. The ROU asset is based on the measurement of the lease liability and also includes any lease payments made prior to or on lease commencement and excludes lease incentives and initial direct costs incurred, as applicable. The lease terms may include options to extend or terminate the lease when it is reasonably certain the Company will exercise any such options. Rent expense for the Company's operating leases is recognized on a straight-line basis over the lease term.

The Company has lease agreements with lease and non-lease components. The Company has elected to not separate lease and non-lease components for any leases within its existing classes of assets and, as a result, accounts for the lease and non-lease components as a single lease component. The Company has also elected to not apply the recognition requirement to any leases within its existing classes of assets with a term of 12 months or less.

Basis of Preparation

The accompanying unaudited interim condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America, or U.S. GAAP, and applicable rules and regulations of the SEC regarding interim financial reporting. As permitted under those rules, certain footnotes or other financial information that are normally required by U.S. GAAP have been condensed or omitted, and accordingly the balance sheet as of December 31, 2018 has been derived from audited financial statements at that date but does not include all of the information required by U.S. GAAP for complete financial statements. These unaudited interim condensed consolidated financial statements have been prepared on the same basis as the Company's annual financial statements and, in the opinion of management, reflect all adjustments (consisting only of normal recurring adjustments) that are necessary for a fair presentation of the Company's financial information. The results of operations for the three months ended March 31, 2019 are not necessarily indicative of the results to be expected for the year ending December 31, 2019 or for any other interim period or for any other future year.

The accompanying unaudited interim condensed consolidated financial statements and related financial information should be read in conjunction with the audited financial statements and the related notes thereto for the year ended December 31, 2018 included in the Company's audited financial statements filed in its Annual Report on Form 10-K for the year ended December 31, 2018.

Use of Estimates

The accompanying unaudited interim condensed consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities, as of the date of the financial statements, and the reported amounts of any expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to accrued liabilities, acquisition contingent consideration, income taxes, and stock-based compensation. Management bases its estimates on historical experience, and on various other market-specific relevant assumptions that management believes to be reasonable, under the circumstances. Actual results may differ from those estimates.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents and marketable securities. The Company invests in a variety of financial instruments and in accordance with its investment policy, limits the amount of credit exposure with any one issuer, industry or geographic area for investments other than instruments backed by the U.S. federal government.

Concentration of Manufacturing and Third-Party Services Risk

The Company is subject to certain risks with respect to sources of supply of manufactured materials and drug product for use in its preclinical studies and clinical trials. Due to the technical aspects of manufacturing drug product for gene therapies, there exist few alternative sources of manufacturing. The Company is reliant upon its own internal manufacturing capability and a small number of third-party vendors to produce drug product in sufficient quantities and quality to conduct its research and development activities.

Accounting Pronouncements Adopted in 2019

In June 2018, the FASB issued ASU 2018-07, *Compensation - Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting*, which expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. An entity should apply the requirements of Topic 718 to nonemployee awards except for specific guidance on inputs to an option pricing model and the attribution of cost. The measurement of equity-classified nonemployee awards is fixed at the grant date, and entities would measure the cost of awards subject to a performance condition using the outcome that is probable at the balance sheet date. The Company adopted this standard on January 1, 2019. As a result of adopting this standard, the Company no longer remeasures equity-classified nonemployee awards. The adoption of this new standard did not result in material impact on the Company's condensed consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which establishes a comprehensive new lease accounting model. Under the new guidance, at the commencement date, lessees are required to recognize a lease liability with a corresponding right-of-use (ROU) asset. Effective January 1, 2019, the Company adopted Topic 842 using the modified

retrospective approach provided by ASU 2018-11. Results for reporting periods beginning January 1, 2019 are presented under Topic 842, while prior period amounts were not adjusted and continue to be presented in accordance with the Company's historical accounting under Topic 840, *Leases*. The Company elected certain practical expedients permitted under the transition guidance, including the election to carryforward historical lease classification. The Company also elected the short-term lease practical expedient, which allowed the Company to not recognize leases with a term of less than twelve months on its consolidated balance sheets.

In addition, the Company elected the lease and non-lease components practical expedient, which allowed the Company to calculate the present value of the fixed payments without performing an allocation of lease and non-lease components.

The impact of the adoption of Topic 842 on the accompanying Condensed Consolidated Balance Sheet as of January 1, 2019 was as follows:

	December 31, 2018	Effect of Adoption	January 1, 2019
		(in thousands)	
Operating lease right-of-use assets	$ —	$ 21,669	$ 21,669
Liabilities:			
Operating leases	$ —	$ 2,541	$ 2,541
Deferred rent	$ 456	$ (456)	$ —
Operating lease liabilities - long-term	$ —	$ 24,304	$ 24,304
Deferred rent and asset retirement obligation - long-term	$ 4,935	$ (4,720)	$ 215

Adoption of the new standard resulted in recording operating lease right-of-use assets and operating lease liabilities of approximately $21.1 million and $26.3 million, respectively, on the Company's condensed consolidated balance sheets as of March 31, 2019. However, the adoption of the new standard did not have an impact on the Company's beginning accumulated deficit, statement of operations or cash flows. For additional information regarding the Company's leases, see Note 9 in the notes to the condensed consolidated financial statements.

3. Investments

Investments consist of available-for-sale securities as follows:

	March 31, 2019			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
		(in thousands)		
Money market funds	$ 49,747	$ —	$ —	$ 49,747
Commercial paper	114,105	1	(12)	114,094
Corporate securities	78,231	70	(9)	78,292
U.S. treasury bills	51,288	7	—	51,295
U.S. government agency securities	27,867	3	(2)	27,868
U.S. agency bonds	32,732	9	—	32,741
U.S. agency discount securities	10,999	—	—	10,999
Total available-for-sale securities	$ 364,969	$ 90	$ (23)	$ 365,036

	December 31, 2018			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(in thousands)			
Money market funds	$ 33,399	$ —	$ —	$ 33,399
Commercial paper	144,578	—	—	144,578
Corporate securities	82,670	8	(39)	82,639
U.S. treasury bills	60,573	—	(8)	60,565
U.S. government agency securities	15,219	—	—	15,219
U.S. agency bonds	51,411	—	(22)	51,389
U.S. agency discount securities	18,716	—	—	18,716
Total available-for-sale securities	$ 406,566	$ 8	$ (69)	$ 406,505

The Company does not intend to sell the investments that are in an unrealized loss position, and it is unlikely that it will be required to sell the investments before recovery of their amortized cost basis, which may be maturity. The Company determined that the gross unrealized losses on its marketable securities at March 31, 2019 were temporary in nature. Unrealized losses from all marketable securities at March 31, 2019 are not material.

The Company's long-term investments as of March 31, 2019 consist of corporate securities.

4. Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually). Financial instruments include cash and cash equivalents, restricted cash, accounts payable and accrued liabilities that approximate fair value due to their relatively short maturities.

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1 – Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2 – Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3 – Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

Assets Measured at Fair Value

Financial assets subject to fair value measurements on a recurring basis and the level of inputs used in such measurements are as follows:

	March 31, 2019			
	Fair Value Measurements Using			
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Money market funds	$ 49,747	$ 49,747	$ —	$ —
Commercial paper	114,094	—	114,094	—
Corporate securities	78,292	—	78,292	—
U.S. treasury bills	51,295	—	51,295	—
U.S. government agency securities	27,868	—	27,868	—
U.S. agency bonds	32,741	—	32,741	—
U.S. agency discount securities	10,999	—	10,999	—
Total financial assets	$ 365,036	$ 49,747	$ 315,289	$ —

	December 31, 2018			
	Fair Value Measurements Using			
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Money market funds	$ 33,399	$ 33,399	$ —	$ —
Commercial paper	144,578	—	144,578	—
Corporate securities	82,639	—	82,639	—
U.S. treasury bills	60,565	—	60,565	—
U.S. government agency securities	15,219	—	15,219	—
U.S. agency bonds	51,389	—	51,389	—
U.S. agency discount securities	18,716	—	18,716	—
Total financial assets	$ 406,505	$ 33,399	$ 373,106	$ —

The financial assets listed above do not include cash held in the Company's primary operating bank accounts of $10.0 million and $7.8 million as of March 31, 2019 and December 31, 2018, respectively.

Liabilities Measured at Fair Value

The Company's contingent acquisition consideration payable, resulting from the acquisition of Cardiogen Sciences, Inc., or Cardiogen, in August 2015, is estimated using a probability-based income approach utilizing an appropriate discount rate. Key assumptions used by management to estimate the fair value of contingent acquisition consideration payable include estimated probability of occurrence, the estimated timing of when the milestone may be attained and assumed discount period and discount rate, which are Level 3 inputs. Changes in the fair value of the contingent acquisition consideration payable, resulting from management's revision of key assumptions are recorded in research and development expense in the consolidated statement of operations and comprehensive loss. The probability-based income approach used by management to estimate the fair value of the contingent acquisition consideration is most sensitive to changes in the estimated probability of occurrence.

The following is a summary of the contingent acquisition consideration payable recorded in the accompanying consolidated balance sheets:

	Amount
	(in thousands)
Balance, December 31, 2018	$ 2,345
Change in fair value of contingent acquisition consideration payable	(22)
Balance, March 31, 2019	$ 2,323

5. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net, consist of the following:

	March 31, 2019	December 31, 2018
	(in thousands)	
Furniture and office equipment	$ 1,968	$ 1,898
Computer equipment	1,219	1,019
Software	513	513
Leasehold improvements	22,917	19,607
Laboratory equipment	10,007	9,570
Manufacturing equipment	6,723	6,619
Construction in progress and deposits on equipment	3,559	3,320
Total property and equipment	46,906	42,546
Less accumulated depreciation and amortization	(12,175)	(10,447)
Property and equipment, net	$ 34,731	$ 32,099

Property and equipment depreciation and amortization expense for the three months ended March 31, 2019 and 2018 was $1.7 million and $1.1 million, respectively.

Accrued Liabilities

Accrued liabilities consist of the following:

	March 31, 2019	December 31, 2018
	(in thousands)	
Accrued payroll and related expenses	$ 5,034	$ 8,581
Accrued research and development expenses	4,877	3,317
Accrued property and equipment	623	71
Accrued professional services	680	783
Other	306	176
Total accrued liabilities	$ 11,520	$ 12,928

6. Commitments and Contingencies

During the three months ended March 31, 2019, the Company entered into an exclusive license agreement with Nationwide Children's Hospital related the Company's AT702 program. Pursuant to the agreement, the Company paid an upfront fee of $7.0 million and will be obligated to make certain milestone and royalty payments upon the achievement of developmental, regulatory and net sales milestones.

As of March 31, 2019, the Company is subject to contingent payments upon the achievement of certain development, regulatory and commercial milestones, totaling up to approximately $275.1 million across all of its licensing agreements. Of this amount, $77.9 million relates to the Company's Crigler-Najjar and *CASQ2*-CPVT programs, for which the Company announced plans to explore outlicensing opportunities to continue development activities.

7. Stock Compensation

Stock-based Compensation Expense

Stock-based compensation expense by category was as follows for the three months ended March 31, 2019 and 2018:

	Three Months Ended March 31,	
	2019	2018
	(in thousands)	
Research and development	$ 3,215	$ 2,055
General and administrative	2,285	1,330
Total stock-based compensation expense	$ 5,500	$ 3,385

The following table summarizes option activity for the three months ended March 31, 2019:

	Number of Options Outstanding	Weighted-Average Exercise Price Per Option	Weighted-Average Remaining Contract Term (Years)	Aggregate Intrinsic Value
				(in thousands)
Balance, December 31, 2018	4,894,201	$ 18.79	7.97	$ 30,235
Options granted	1,248,000	$ 25.66		
Options exercised	(213,891)	$ 14.05		
Options forfeited	(69,456)	$ 26.37		
Balance, March 31, 2019	5,858,854	$ 20.34	8.15	$ 109,622
Exercisable, March 31, 2019	2,316,213	$ 13.08	7.17	$ 60,086
Vested and expected to vest, March 31, 2019	5,483,592	$ 19.89	8.09	$ 105,047

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value of the Company's common stock as of March 31, 2019. During the three months ended March 31, 2019, options to purchase 213,891 shares of common stock with an intrinsic value of approximately $3.8 million were exercised, generating approximately $3.0 million of cash received.

The weighted average grant date fair value of employee options granted during the three months ended March 31, 2019 and 2018 was $16.03 and $21.81 per share, respectively. As of March 31, 2019, the total unrecognized compensation expense related to unvested employee options, net of estimated forfeitures, was approximately $55.8 million, which the Company expects to recognize over an estimated weighted average period of 2.67 years. To the extent the actual forfeiture rate is different from what the Company has estimated, stock-based compensation related to these awards will be different from its expectations.

The fair value of stock options granted to employees was estimated using a Black-Scholes option pricing model with the following assumptions:

	Three Months Ended March 31,	
	2019	2018
Expected term (in years)	5.5-6.1	5.8-6.1
Expected volatility	68%	75-76%
Risk-free interest rate	2.3-2.6%	2.3-2.7%
Expected dividend yield	—%	—%

Restricted Stock Units

In January 2019, the Company's compensation committee of the board of directors approved the commencement of granting restricted stock units, or RSUs, to our employees. RSUs are share awards that entitle the holder to receive freely tradable shares of the Company's common stock upon the completion of a specific period of continued service. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. RSUs granted are valued at the market price of

the Company's common stock on the date of grant. The Company recognizes stock-based compensation expense for the fair value of RSUs on a straight-line basis over the requisite service period of these awards.

The following table summarizes activity of RSUs granted to employees with service-based vesting during the three months ended March 31, 2019:

	Number of RSUs Outstanding	Weighted-Average Grant Date Fair Value Per RSU
Balance, December 31, 2018	—	
RSUs granted	418,819	$ 25.66
RSUs vested	—	
RSUs forfeited	(3,825)	$ 24.74
Balance, March 31, 2019	414,994	$ 25.67

2016 Employee Stock Purchase Plan

On July 19, 2016, the 2016 Employee Stock Purchase Plan, or the 2016 ESPP was adopted. The Company initially reserved 210,000 shares of common stock for issuance under the 2016 ESPP. The number of shares reserved for issuance under the 2016 ESPP will increase automatically on January 1 of each calendar year beginning after the first offering date and continuing through the first ten calendar years by the number of shares equal to 1% of the total outstanding shares of the Company's common stock as of the immediately preceding December 31.

The 2016 ESPP commenced on May 1, 2018. Under the 2016 ESPP, employees may purchase common stock through payroll deductions at a price equal to 85% of the lower of the fair market value at the beginning of the offering period or at the end of each applicable purchase period. The 2016 ESPP generally provides for offering periods of six months in duration with purchase periods ending on either May 15 or November 15. Contributions under the 2016 ESPP are limited to a maximum of 15% of an employee's eligible compensation and purchases are settled with common stock from the ESPP's previously authorized and available pool of shares. The expense for the three months ended March 31, 2019 was based on the fair value of rights granted upon the commencement of an offering and calculated using the following assumptions: expected term in years is 0.5; volatility is 62.2%; the risk-free interest rate is 2.50%; and no dividend yield.

8. Income Taxes

The Company did not record a federal or state income tax provision or benefit for the three months ended March 31, 2019 and 2018 as it has incurred net losses since inception. In addition, the net deferred tax assets generated from net operating losses have been fully reserved as the Company believes it is not more likely than not that the benefit will be realized.

9. Leases

Under Topic 842, operating lease expense is generally recognized evenly over the term of the lease. The Company has various non-cancelable lease agreements for our office and manufacturing spaces with lease periods expiring between 2023 and 2027. The Company's lease terms may include options to extend or terminate the leases. The lease term represents the period up to the early termination date unless it is reasonably certain that the Company will not exercise the early termination option. For certain leases, the Company has options to extend the lease term for additional periods ranging from five to eight years. These renewal options are not considered in the remaining lease term unless it is reasonably certain that the Company will exercise such options. Certain leases include rental payments that are adjusted periodically based on changes in consumer price and other indices.

Leases with an initial term of twelve months or less are not recorded on the condensed consolidated balance sheets. For lease agreements entered into or reassessed after the adoption of Topic 842, the Company combined the lease and non-lease components in determining the lease liabilities and ROU assets.

The Company's lease agreements generally do not provide an implicit borrowing rate, therefore an internal incremental borrowing rate is determined based on information available at lease commencement date for purposes of determining the present value of lease payments. The Company used the incremental borrowing rate on January 1, 2019 for all leases that commenced prior to that date.

For the three months ended March 31, 2019, the Company recorded operating lease costs of $1.4 million. As of March 31, 2019, maturities of lease liabilities for the following five fiscal years and thereafter were as follows (in thousands except lease term and discount rate):

		Amount
Remainder of 2019	$	4,214
2020		5,791
2021		5,973
2022		6,174
2023		4,863
Thereafter		10,086
Total lease payments		37,101
Less:		
Imputed interest		(10,633)
Tenant improvement not yet received		(176)
Present value of operating lease liabilities	$	26,292
Current operating lease liabilities	$	2,773
Operating lease liabilities - long-term	$	23,519
Weighted-average remaining lease term (in years)		6.4
Weighted-average discount rate		10.9%
Additional lease not yet commenced (undiscounted)		
Operating lease liability to commence May 2019	$	7,854

As the Company elected to apply the provisions of Topic 842 on a prospective basis, the following comparative period disclosure is being presented in accordance with Topic 840. The future minimum commitments under the Company's leases as of December 31, 2018, were as follows:

		Amount
		(in thousands)
2019	$	6,073
2020		6,692
2021		6,901
2022		7,130
2023		5,847
Thereafter		13,024
Total minimum lease payments	$	45,667

10. Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period and excludes any potential dilutive effects of common stock equivalents. Diluted net loss per share is computed giving effect to all potential dilutive common shares, including common stock issuable upon exercise of stock options, convertible preferred stock, and unvested restricted common stock. As the Company had net losses for the three months ended March 31, 2019 and 2018, all potential common shares were determined to be anti-dilutive and were therefore excluded from the calculation of diluted net loss per share.

The following table sets forth the computation of basic and diluted net loss per share of common stock during the three months ended March 31, 2019 and 2018:

	Three Months Ended March 31,	
	2019	2018
	(in thousands, except per share data)	
Net loss	$ (49,391)	$ (25,571)
Weighted-average number of shares used in computing net loss per share	43,625,316	34,582,071
Net loss per share, basic and diluted	$ (1.13)	$ (0.74)

The following outstanding shares of common stock equivalents were excluded from the computation of diluted net loss per share of common stock for the periods presented because including them would have been anti-dilutive:

	Three Months Ended March 31,	
	2019	2018
Stock options to purchase common stock	5,858,854	4,902,872
Restricted stock units	414,994	—
Common stock warrants	—	9,914
	6,273,848	4,912,786

11. Related Party Transactions

There were no material related party transactions during the three months ended March 31, 2019 and 2018.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

NOTE ABOUT FORWARD-LOOKING STATEMENTS

This quarterly report contains forward-looking statements. All statements other than statements of historical fact are "forward-looking statements" for purposes of this Quarterly Report on Form 10-Q. These forward-looking statements may include, but are not limited to, statements regarding our future results of operations and financial position, business strategy, market size, potential growth opportunities, timing and results of preclinical and clinical development activities, and potential regulatory approval and commercialization of product candidates. In some cases, forward looking-statements may be identified by terminology such as "believe," "may," "will," "should", "predict", "goal", "strategy", "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect," "seek" and similar expressions and variations thereof. These words are intended to identify forward-looking statements. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in the "Risk Factors" section and elsewhere in this Quarterly Report on Form 10-Q. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, 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 we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

Investors should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this report to conform these statements to actual results or to changes in our expectations, except as required by law.

As used in this Quarterly Report on Form 10-Q, the terms "Audentes," "the Company," "we," "us," and "our" refer to Audentes Therapeutics, Inc. and, where appropriate, its consolidated subsidiaries, unless the context indicates otherwise.

Investors should read the following discussion and analysis of our financial condition and results of operations together with our unaudited condensed consolidated financial statements and related notes included in Part I, Item 1 of this report and with our audited consolidated financial statements and related notes thereto for the year ended December 31, 2018, included in our Annual Report on Form 10-K.

Business Overview

We are a leading AAV-based genetic medicines company focused on developing and commercializing innovative products for patients living with serious rare neuromuscular diseases. We are leveraging our adeno-associated viral vector, or AAV, gene therapy technology platform and proprietary manufacturing expertise to develop programs across three modalities: gene replacement, vectorized exon skipping and vectorized RNA knockdown.

We have built a compelling portfolio of product candidates targeting rare neuromuscular diseases, including X-Linked Myotubular Myopathy, or XLMTM, Pompe disease, Duchenne muscular dystrophy, or DMD, and myotonic dystrophy type 1, or DM1. We have an ongoing Phase 1/2 clinical trial of our most advanced product candidate, AT132 for the treatment of XLMTM. In our Pompe disease program we are currently conducting IND-enabling preclinical studies and plan to submit an investigational new drug application, or IND, in the third quarter of 2019. In our DMD program, we are collaborating with Nationwide Children's Hospital, or Nationwide Children's, to develop AT702, a vectorized exon skipping product candidate designed to induce exon 2 skipping in DMD patients with duplications of exon 2 and mutations in exons 1-5 of the dystrophin gene. We plan to commence a Phase 1/2 clinical trial of AT702 at Nationwide Children's in the fourth quarter of 2019. Separate from the Nationwide Children's collaboration, we are conducting preclinical work to advance AT751 and AT753, vectorized exon skipping product candidates to treat DMD patients with genotypes amenable to exon 51 and exon 53 skipping. In combination, we estimate that AT702, AT751 and AT753 may have the potential to address more than 25% of DMD patients, and we plan to leverage our vectorized exon skipping platform to develop additional product candidates with the potential to address up to 80% of DMD patients over time. We are also working with Nationwide Children's to evaluate vectorized RNA knockdown and vectorized exon skipping for DM1. Preclinical studies are underway, and we expect to submit an IND for AT466 in 2020. We maintain full global rights to all of our product candidates.

We have developed a proprietary in-house current Good Manufacturing Practices, or cGMP, capability to produce our product candidates, providing us with a core strategic capability, and enabling more control over development timelines, costs and intellectual property. Our manufacturing facility is located in South San Francisco and supports our process and analytical development, fill-finish, quality control testing and manufacturing operations in accordance with cGMP requirements. We have designed and commissioned the facility to support the unique licensing requirements as promulgated by both the U.S Food and Drug Administration, or FDA, and European Medicines Agency, or EMA, and we have initiated Biologic License Application, or BLA, readiness and validation activities for our XLMTM program. Operating at a 1,000-liter scale, we believe our current manufacturing capacity is sufficient to meet the anticipated global commercial demands of our XLMTM program, and the near-term development needs of our other product candidates. Additionally, we have the ability to add up to 8,000 liters of additional capacity within our existing lease footprint. We plan to continue investment in these capabilities to maintain our manufacturing leadership and enable the cost-effective production of high-quality AAV vectors to support our clinical development and commercialization activities.

Recent Developments

AAV Technology Platform and Pipeline Expansion

In April 2019, we announced the expansion of our scientific platform and product pipeline with new product candidates that employ our vectorized antisense technology for the treatment of DMD and DM1. This approach combines the delivery power of AAV with the precision tools of antisense oligonucleotides, or ASOs, to develop potential best-in-class therapeutic candidates for these devastating neuromuscular diseases. To develop these promising new programs, we entered into an exclusive license agreement and plan to collaborate with Nationwide Children's. Upon entry into the licensing agreement, we paid Nationwide Children's an upfront payment of $7.0 million and will be obligated to pay certain milestone and royalty payments upon the achievement of developmental and sales milestones.

Vectorized exon skipping uses an AAV vector to deliver an antisense sequence designed to induce cells to skip over faulty or misaligned sections of genetic code, leading to the expression of a more complete, functional protein. For the treatment of DMD, we believe this approach has the potential to provide significant advantages over microdystrophin gene replacement strategies that produce a substantially truncated protein, which may limit the degree and durability of disease correction, as well as existing ASO therapies, whose efficacy is limited by poor biodistribution to muscle tissue. We are collaborating with Nationwide Children's to develop AT702, an AAV-antisense candidate designed to induce exon 2 skipping for DMD with duplications of exon 2 and mutations in exons 1-5 of the dystrophin gene. In preclinical studies of mice with exon 2 duplications, AT702 demonstrated robust proof-of-concept with dose-dependent increases in production of wild type or near-wild type length dystrophin protein and improvements in muscle function. We are currently conducting additional preclinical work and expect to commence a Phase 1/2 clinical trial at Nationwide Children's in the fourth quarter of 2019.

Separate from the Nationwide Children's collaboration, we are conducting preclinical work to advance AT751 and AT753, additional vectorized exon skipping candidates, to treat DMD patients with genotypes amenable to exon 51 and exon 53 skipping. Both AT751 and AT753 utilize the same vector construct backbone as AT702, enabling a potentially accelerated path into clinical development. With these initial programs, we are targeting more than 25% of patients with DMD, and we plan to leverage our vectorized exon skipping platform to develop further product candidates to address up to 80% of DMD patients over time.

In addition, we are working with Nationwide Children's to evaluate vectorized RNA knockdown and vectorized exon skipping approaches for DM1. Both approaches are designed to prevent the accumulation of toxic dystrophia myotonica-protein kinase, or DMPK, RNA in affected cells, thereby restoring normal cellular function. RNA knockdown and exon skipping have both been clinically validated in studies with ASOs. As with DMD, we believe combining these approaches with AAV delivery can overcome the biodistribution limitations of ASO-based therapies. Preclinical studies are underway, and we expect to submit an IND for the selected product candidate, AT466, in 2020.

ASPIRO Phase 1/2 clinical trial of AT132 in XLMTM

In May 2019, we presented new positive data from ASPIRO at the 22nd Annual Meeting of the American Society of Gene and Cell Therapy. The newly reported data included safety and efficacy assessments for 11 patients enrolled in ASPIRO as of the April 8, 2019 data cut-off date, including 48 weeks of follow-up for seven patients enrolled in Cohort 1 ($1x10^{14}$ vector genomes per kilogram, or vg/kg; six treated and one untreated control) and 24 weeks of follow-up for four patients in Cohort 2 ($3x10^{14}$ vg/kg; three treated and one untreated control). Key assessments include neuromuscular function as measured by both improvements in the CHOP INTEND score and the achievement of motor milestones; respiratory function as measured by improvements in maximal inspiratory pressure, or MIP, and reduction in ventilator dependence; and vector copy number, mRNA, protein expression and histological improvement as assessed via muscle biopsy.

Efficacy results

Rapid CHOP INTEND improvements were achieved and maintained in both dose cohorts, and the majority of patients demonstrated progressive attainment of motor developmental milestones, such as head control, sitting unassisted, crawling, standing with support and initiating stepping movements. Patients receiving AT132 have achieved reductions in ventilator dependence not previously observed in chronically ventilated patients with neuromuscular disorders. Reduction of ventilator dependence is an endpoint considered to be correlated with survival. Four patients were successfully weaned off of ventilation by the 48-week timepoint, with all other treated patients demonstrating sustained and clinically meaningful reductions in ventilator use.

Muscle biopsy data, including vector copy number, mRNA expression, and protein expression showed robust dose-dependent transduction, transcription and protein expression. All biopsies showed marked improvement in histopathological markers of disease, with a trend toward continued improvement in the Cohort 1 patient samples from the 24 to 48-week timepoints, and evidence of more rapid pathological improvement by week 24 in the Cohort 2 biopsy samples.

Safety results

AT132 was generally well-tolerated and showed a manageable safety profile across both dose groups. There were no new possibly or probably treatment-related serious adverse events, or SAEs, reported in Cohort 1. There were eight possibly or probably treatment-related SAEs reported in Cohort 2, including troponin I elevations, creatine kinase elevations, myocarditis, ST segment elevation, atrial tachycardia, hyperbilirubinemia, nausea, vomiting and fever. All SAEs were successfully managed and patients showed no evidence of clinical compromise. Results indicated no clinically meaningful differences in the safety and tolerability profile of AT132 between the $1x10^{14}$ vg/kg and $3x10^{14}$ vg/kg dose cohorts.

Crigler-Najjar and CASQ2-CPVT

We have undertaken a strategic review of our product candidates and plan to focus on those programs that have the potential to provide the greatest long-term value for patients and stockholders. With the addition of the DMD and DM1 product candidates to our pipeline, we plan to focus our future efforts on our rare neuromuscular disease programs, including XLMTM, Pompe disease, DMD and DM1, and explore outlicensing opportunities to continue to advance the important and promising gene therapies for Crigler-Najjar and *CASQ2*-CPVT.

License Agreements

We have built our portfolio of product candidates in part by engaging in license and collaboration agreements as well as strategic transactions with third parties. In July 2013, we entered into a license agreement with REGENXBIO Inc., or REGENXBIO, pursuant to which we obtained intellectual property rights related to AT132 and AT845. Under this arrangement, we are contractually committed to certain payments including (i) up to $8.8 million in combined development and regulatory milestone fees for each indication and each licensed product; (ii) up to $45.0 million in combined commercial milestone fees based on various annual aggregate net sales thresholds; and (iii) certain royalty payments.

Financial Overview

Since our inception, we have devoted substantially all of our resources to: identifying, acquiring, and developing our product candidate portfolio; organizing and staffing our company; raising capital; developing our manufacturing capabilities; and providing general and administrative support for these operations. We have never generated revenue and have incurred significant net losses since inception. We do not expect to receive any revenue from any product candidates that we develop until we obtain regulatory approval and commercialize our product candidates or enter into collaborative agreements with third parties. Our net losses were $128.8 million, $90.2 million and $59.7 million for the years ended December 31, 2018, 2017 and 2016, respectively, and $49.4 million for the three months ended March 31, 2019. As of March 31, 2019, we had an accumulated deficit of $368.9 million. We expect to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- invest significantly to further develop and seek regulatory approval for our existing product candidates;
- continue to develop our proprietary in-house manufacturing facility and capabilities;
- hire additional clinical, scientific, management and administrative personnel;
- seek regulatory and marketing approvals for any product candidates that we may develop;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any drugs for which we may obtain marketing approval;

- maintain, expand and protect our intellectual property portfolio;
- further expand our pipeline of potential product candidates;
- acquire or in-license other assets and technologies; and
- add additional operational, financial and management information systems and processes to support our ongoing development efforts, any future manufacturing or commercialization efforts and our administrative and compliance obligations as a public company.

We have funded our operations to date primarily from the issuance and sale of our convertible preferred stock, through the issuance and sale of our common stock pursuant to public offerings. As of March 31, 2019, we had cash, cash equivalents and marketable securities of $375.0 million, which includes approximately $5.5 million of long-term investments.

To fund our current operating plans, we will need additional capital, which we may obtain through one or more equity offerings, debt financings or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our preclinical and clinical development efforts. There can be no assurance that we will ever be profitable or generate positive cash flow from operating activities.

Financial Operations Overview

Research and Development Expenses

Research and development direct program expenses consist primarily of external costs incurred for the development of our product candidates, which include:

- expenses incurred under agreements with consultants, third-party service providers and investigative clinical trial sites that conduct research and development activities on our behalf;
- laboratory and vendor expenses related to the execution of preclinical studies and clinical trials;
- costs related to production of preclinical and clinical materials, including fees paid to contract manufacturers and manufacturing input costs for use in internal manufacturing processes; and
- costs related to in-licensing of rights to develop and commercialize our product candidate portfolio.

Personnel, non-program and unallocated program expenses include costs associated with activities performed by our internal research and development organization and generally benefit multiple programs. These costs are not allocated by product candidate and consist primarily of:

- personnel costs, which include salaries, benefits and stock-based compensation expense;
- facilities and other expenses, which include expenses for rent and maintenance of facilities, depreciation and amortization expense;
- lab supplies and equipment used for internal research and development activities;
- unallocated manufacturing expenses; and
- the change in fair value of contingent acquisition consideration payable.

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks performed by others using information and data provided to us by our vendors, collaborators and third-party service providers. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and as services are performed.

The largest component of our operating expenses has historically been our investment in research and development activities. We do not allocate personnel and other costs, such as salaries, benefits, stock-based compensation expense and certain internal program costs to product candidates on a program-specific basis.

The following table summarizes our research and development expenses incurred during the respective periods:

	Three Months Ended March 31,	
	2019	2018
	(in thousands)	
AT132 direct program costs	$ 5,708	$ 2,520
AT845 direct program costs	3,900	2,168
AT466 direct program costs	348	—
AT702 direct program costs	7,308	—
AT342 direct program costs	391	1,294
Personnel, non-program, and unallocated program costs[1]	22,182	13,909
Total research and development expenses	$ 39,837	$ 19,891

(1) Includes $0.3 million of costs related to our AT307 program three months ended March 31, 2018. In the first quarter of 2019, we decided to seek a third-party to develop the AT307 program. The costs we incurred for the AT307 program during the three months ended March 31, 2019 were immaterial.

We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, including investments in manufacturing, as our programs advance into later stages of development and as we conduct clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel costs, facilities costs, including rent and maintenance of facilities, depreciation and amortization expense and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, bonuses, payroll taxes, benefits and stock-based compensation expense. We expect our general and administrative expenses to increase for the foreseeable future due to anticipated increases in headcount to advance and support the development of our product candidates and as a result of our operations as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, The Nasdaq Global Market, and other governing bodies in addition to insurance expenses, investor relations activities and other administration, accounting and professional services.

Interest Income

Interest income consists of interest earned on our cash, cash equivalents and investments.

Other Income (Expense), Net

Other income (expense), net primarily consists of gains and losses on disposals of property and equipment, investment management fees and foreign currency transaction gains and losses incurred during the period.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our 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 believe that the accounting policies related to business combinations and contingent consideration payable are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Our critical accounting policies and estimates are detailed in the Management's Discussion and Analysis of Financial Condition and Operations included in our Annual Report on Form 10-K for the year ended December 31, 2018. Significant

changes to our accounting policies as a result of adopting Topic 842, *Leases*, are discussed in Note 2, *Summary of Significant Accounting Policies*, to the Unaudited Interim Condensed Consolidated Financial Statements.

Recent Accounting Pronouncements

Except as described in Note 2, *Summary of Significant Accounting Policies*, to the Unaudited Interim Condensed Consolidated Financial Statements, there have been no new accounting pronouncements or changes to accounting pronouncements during the three months ended March 31, 2019, as compared to the recent accounting pronouncements described in our Annual Report on Form 10-K for the year ended December 31, 2018, that are significant to us.

Results of Operations

Comparison of the Three Months Ended March 31, 2019 and 2018

	Three Months Ended March 31,		
	2019	2018	Change
	(in thousands)		
Operating expenses			
Research and development	$ 39,837	$ 19,891	$ 19,946
General and administrative	11,993	6,519	5,474
Total operating expenses	51,830	26,410	25,420
Loss from operations	(51,830)	(26,410)	(25,420)
Interest income, net	2,472	859	1,613
Other expense, net	(33)	(20)	(13)
Net loss	$ (49,391)	$ (25,571)	$ (23,820)

Research and Development

Research and development expenses increased by $19.9 million, or 100%, to $39.8 million for the three months ended March 31, 2019. The increase was primarily the result of a $6.7 million increase in license and milestone payments, primarily due to the in-licensing of AT702, a $3.9 million increase for facilities and overhead related costs primarily due to increased headcount and investment in manufacturing, a $3.5 million increase in manufacturing supplies expense, a $3.2 million increase in personnel costs, a $1.2 million increase for non-cash stock-based compensation expense due to increased headcount to support our growth and increasing fair values for stock option awards, a $0.9 million increase in consulting and professional services, and a $0.5 million increase in clinical trials cost.

Our AT132 and AT845 program expenses increased by $3.2 million and $1.7 million, respectively, as we increased manufacturing of study materials and incurred additional consulting and initiation costs in preparation for planned clinical trials. In connection with the in-licensing of AT702, we incurred a one-time license fee of $7.0 million and $0.3 million in development expense during the three months ended March 31, 2019. Additionally, we initiated development activities for our AT466 program and incurred $0.3 million in expense during the three months ended March 31, 2019.

General and Administrative

General and administrative expenses increased by $5.5 million, or 84%, to $12.0 million for the three months ended March 31, 2019. The increase was primarily the result of a $1.0 million increase in stock-based compensation expense due to increased headcount and increasing fair values for stock option awards, a $0.8 million increase in personnel due to an increased headcount, a $0.8 million increase in consulting expense and professional services and a $2.8 million increase for facilities and overhead related costs to support our continued growth.

Interest Income, net

Interest income, net increased by $1.6 million, or 188%, to $2.5 million for the three months ended March 31, 2019, primary due to a higher cash balance as compared to the three months ended March 31, 2018 and our investment of funds received from our public equity offerings in fixed-income securities.

Liquidity, Capital Resources and Plan of Operations

We are not profitable and have incurred losses and negative cash flows from operations each year since our inception. Our operations have been financed primarily by net proceeds from the sale and issuance of convertible preferred stock and common stock.

Our primary use of cash is to fund operating expenses, which consist of research and development expenditures and general and administrative expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We believe that our existing cash, cash equivalents and investments will be sufficient to meet our anticipated cash and capital expenditure requirements through at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We will continue to require additional financing to advance our product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms, or at all. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies.

Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development and manufacturing activities. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated product development programs.

If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If additional funding is required, there can be no assurance that additional funds will be available to us on acceptable terms on a timely basis, if at all. If we are unable to raise capital, we will need to curtail planned activities to reduce costs. Doing so will likely have an unfavorable effect on our ability to execute our business plans.

The following table summarizes our cash flows for the periods indicated:

	Three Months Ended March 31,	
	2019	2018
	(in thousands)	
Cash used in operating activities	$ (42,220)	$ (24,592)
Cash provided by (used in) investing activities	28,026	(1,440)
Cash provided by financing activities	3,005	217,929
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (11,189)	$ 191,897

Cash Flows from Operating Activities

Cash used in operating activities for the three months ended March 31, 2019 was $42.2 million. Our net loss was $49.4 million, which was partially offset by noncash charges of $6.7 million, consisting primarily of $5.5 million of stock-based compensation expense and $1.7 million of depreciation and amortization expense, offset by $1.1 million primarily related to the accretion of discounts on marketable securities. The changes in our net operating assets and liabilities were primarily the result of a decrease in prepaid expenses and current assets of $1.8 million, an increase of $1.9 million in accounts payable and a decrease of $2.6 million in accrued liabilities. These changes are primarily based on timing of invoicing by our vendors and payments from us to them.

Cash used in operating activities for the three months ended March 31, 2018 was $24.6 million. Our net loss was $25.6 million, which was partially offset by noncash charges of $2.2 million, consisting primarily of $3.4 million of stock-based compensation expense, $1.1 million of depreciation and amortization expense, and a $2.3 million reduction in the fair value of the contingent acquisition consideration liability. The change in our net operating assets was primarily the result of a decrease in our accrued liabilities of $2.2 million, offset by an increase in accounts payable of $0.6 million and a decrease in prepaid expenses of

$0.3 million. These decreases in accrued liabilities are based on timing of invoicing for services, primarily for research and development expenses.

Cash Flows from Investing Activities

Cash provided by investing activities was $28.0 million for the three months ended March 31, 2019, primarily due to purchases of investments of $117.5 million and purchases of property, equipment and leasehold improvements of $1.3 million, offset by the proceeds of $146.8 million from the maturities of investments.

Cash used in investing activities was $1.4 million for the three months ended March 31, 2018, primarily due to purchases of property and equipment of $0.9 million and investments of $35.3 million, partially offset by the proceeds of $34.8 million from the maturities of investments.

Cash Flows from Financing Activities

Cash provided by financing activities for the three months ended March 31, 2019 was related to proceeds of $3.0 million from the exercise of stock options.

Cash provided by financing activities for the three months ended March 31, 2018 were related to proceeds of $0.8 million from the exercise of stock options and net proceeds of $217.1 million from our follow-on offering.

Off-Balance Sheet Arrangements

At March 31, 2019, we were not a party to any off-balance sheet arrangements that have, or are reasonably likely to have, a current or future effect on our financial condition, changes in financial condition, revenue or expenses, results of operations, liquidity, capital expenditures or capital resources.

Contractual Obligations and Other Commitments

Lease Agreements

There were no significant changes to our lease agreements during the three months ended March 31, 2019 as compared to our previous disclosure in our Annual Report on Form 10-K for the year ended December 31, 2018.

License and Collaboration Agreements

During the three months ended March 31, 2019, the Company entered into an exclusive license agreement with Nationwide Children's Hospital related the Company's AT702 program. Pursuant to the agreement, the Company paid an upfront fee of $7.0 million and will be obligated to make certain milestone and royalty payments upon the achievement of developmental, regulatory and net sales milestones.

As of March 31, 2019, the Company is subject to contingent payments upon the achievement of certain development, regulatory and commercial milestones, totaling up to approximately $275.1 million across all of its licensing agreements. Of this amount, $77.9 million relates to the Company’s Crigler-Najjar and *CASQ2*-CPVT programs, for which the Company announced plans to explore outlicensing opportunities to continue development activities.

Other Contracts

We also enter into contracts in the normal course of business with various third parties for services related to preclinical research studies, clinical trials, testing, manufacturing and other services. These contracts generally provide for termination upon notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

ITEM 3. QUALITATIVE AND QUANTITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We had cash, cash equivalents and investments of $375.0 million and $414.3 million as of March 31, 2019 and December 31, 2018, respectively, which consisted of bank deposits, money market funds and marketable fixed income securities. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant for us. We had no debt outstanding as of March 31, 2019 or December 31, 2018.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on that evaluation, our Chief

Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of March 31, 2019.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the first quarter of 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II

ITEM 1. LEGAL PROCEEDINGS

We are not currently a party to any pending legal proceedings. From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm and other factors.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. Investors should carefully consider the risks described below, as well as the other information in this report, including our unaudited interim condensed consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. This list is not exhaustive and the order and presentation does not reflect management's determination of priority or likelihood. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and investors may lose all or part of their investment.

Risks Related to Product Development and Regulatory Approval

We are early in our development efforts. If we are unable to develop, obtain regulatory approval for and commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We have invested substantially all of our efforts and financial resources in the identification and development of our AAV gene therapy technology platform and our portfolio of product candidates, which target a range of rare neuromuscular diseases, including X-Linked Myotubular Myopathy, or XLMTM, Pompe disease, Duchenne muscular dystrophy, or DMD, and myotonic dystrophy type 1, or DM1. Our ability to generate product revenue, which we do not expect will occur for several years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product.

Each of our programs and product candidates will require preclinical and clinical development, regulatory approval in multiple jurisdictions, obtaining preclinical, clinical and commercial manufacturing supply, capacity and expertise, building of a commercial organization, significant marketing efforts and substantial investment to achieve all of the foregoing before we generate any revenue from product sales. Our product candidates must be authorized for marketing by the U.S. Food and Drug Administration, or the FDA, or certain other foreign regulatory agencies, such as the European Medicines Agency, or EMA, before we may commercialize our product candidates.

The success of our product candidates depends on multiple factors, including:

- successful completion of preclinical studies, including those compliant with Good Laboratory Practices, or GLP, toxicology studies, biodistribution studies and minimum effective dose studies in animals;
- effective investigational new drug applications, or INDs, or Clinical Trial Authorizations, or CTAs, that allow commencement of our planned clinical trials or future clinical trials for our product candidates in relevant territories;
- successful enrollment and completion of clinical trials compliant with current Good Clinical Practices, or GCPs;
- positive results from our clinical programs that are supportive of safety and efficacy and provide an acceptable risk-benefit profile for our product candidates in the intended patient populations;
- receipt of regulatory approvals from applicable regulatory authorities;
- continued successful development of our internal manufacturing processes, including process development and scale-up activities to supply drug product for preclinical studies, clinical trials and commercial sale;
- establishment of arrangements with third-party contract manufacturing organizations, or CMOs, for key materials used in our manufacturing processes and to establish backup sources for clinical and large-scale commercial supply;
- establishment and maintenance of patent and trade secret protection and regulatory exclusivity for our product candidates;
- enforcement and defense of intellectual property rights and claims;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;

- acceptance of our product candidates, if and when approved, by patients and the medical community;
- our effective competition against other therapies available in the market;
- establishment and maintenance of adequate reimbursement from third-party payors for our products; and
- maintenance of a continued acceptable safety profile of our product candidates following approval.

If we do not succeed in one or more of these factors in a timely manner, or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Success in early preclinical studies or clinical trials may not be indicative of results obtained in later preclinical studies and clinical trials and does not ensure regulatory approval of our product candidates.

Though viral vectors similar to ours have been evaluated by others in clinical trials, our product candidates only recently entered into human clinical trials, and we may experience unexpected or adverse results in the future. We will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates are safe and effective, with a favorable risk-benefit profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. Trial designs and results from previous trials are not necessarily predictive of our future clinical trial designs or results, and if we report interim safety and efficacy results from an ongoing clinical trial, we may not be able to confirm these results upon full analysis of the complete trial data. For example, in ASPIRO, an ongoing Phase 1/2 clinical trial of AT132 in XLMTM patients, we have reported encouraging interim data. However, the interim dataset from ASPIRO will differ from the final datasets upon which global regulatory decisions will be based. Potential reasons for these differences include, but are not limited to:

- interim datasets may be comprised of a small number of patients, and the safety and efficacy results from longer term follow-up in patients dosed earlier in the study, or results from future patients, may not replicate those early results;
- interim datasets may be comprised of patients evaluated at a specific dose level, whereas patients enrolled later in a study may receive higher doses with unknown implications for safety and efficacy;
- not all patients may demonstrate improvement;
- patients may discontinue their involvement in ASPIRO for a number of reasons, including disease progression or a lack of clinical benefit, and discontinuations will impact the amount of data we collect over time;
- additional time and patient accrual provide new opportunities to capture new adverse events and further characterize the safety and efficacy of AT132; and
- the precise composition of the final datasets is subject to ongoing regulatory feedback, which is likely to continue up until the time of submission of a biologics license application, or BLA, or equivalent, and the advice may vary by regulatory authority.

In addition, the safety and efficacy results we observe with our product candidates in preclinical animal models may not be predictive of results from our clinical trials in humans, or may not translate to humans until higher doses are utilized, if at all.

Many companies in the biotechnology industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and there is a high failure rate for product candidates proceeding through clinical trials. Our product candidates may fail in late-stage clinical development if they do not show the desired safety and efficacy, even if they have successfully advanced through initial clinical trials. In addition, data obtained from preclinical studies and clinical trials are subject to varying interpretations. If agencies such as the FDA or EMA interpret data from our development programs differently than we do, the regulatory approval of our product candidates may be delayed, limited or prevented.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate for licensure. Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested, or they may impose significant limitations in the form of narrow indications, warnings or a Risk Evaluation and Mitigation Strategy, or REMS. These regulatory authorities may require precautions or contra-indications with respect to conditions of use or they may

grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially and adversely affect our business, financial condition, results of operations and prospects.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our product candidates may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, manufacturing and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of preclinical studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are, and will be, based on a variety of assumptions. The actual timing of achieving these milestones can vary significantly compared to our estimates, in some cases for reasons beyond our control. We may experience numerous unforeseen events during, or as a result of, any clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- the FDA and other governmental health authorities, Institutional Review Boards, or IRBs, or ethics committees may not authorize or may delay authorizing us or our investigators to commence a clinical trial or conduct a clinical trial at all or at a prospective trial site, such as by requiring us to conduct additional preclinical studies and to submit additional data or imposing other requirements before permitting us to initiate or continue a clinical trial. For example, in early 2019 our collaborators at Nationwide Children's Hospital, or Nationwide Children's, submitted an IND for AT702 to treat DMD in patients with duplications of exon 2 and mutations in exons 1-5 of the dystrophin gene, and the FDA requested additional preclinical work prior to authorizing the initiation of clinical development;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results and we may decide, or regulators may require us, to conduct preclinical studies in addition to those we currently have planned or additional clinical trials or we may decide to abandon drug development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party suppliers and contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to health risks;
- the cost of planned clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other gene therapy studies that raise safety or efficacy concerns broadly about the field of gene therapy, or about our product candidates specifically. For example, we have reported that a series of adverse events have occurred in ASPIRO, the Phase 1/2 clinical trial in patients with XLMTM, several of which have been deemed to be possibly or probably related to treatment with AT132. In our Pompe disease program, we conducted a toxicology study in non-human primates during which we observed an unexpected and dose-dependent safety signal with a prototype version of AT845, which resulted in early termination of the study. We are currently conducting IND-enabling studies of AT845, a redesigned vector for Pompe disease, and plan to submit the IND to the FDA in the third quarter of 2019. Additionally, in January 2018, an academic gene therapy researcher published results from non-GLP studies conducted in a small number of non-human primates and piglets, utilizing AAV vectors with different capsid serotypes and transgenes than those we use in our product candidates. These publications cited concerns about the potential risks of high systemic doses of AAV gene therapy products. We have not observed similar results in any of our non-clinical studies with our candidate vectors, and continue to conduct

preclinical studies and clinical trials across our portfolio of product candidates. If we observe unexpected safety signals in these studies or trials, we may decide, or regulatory authorities may require us, to delay or halt further development of our product candidates.

Our product candidates are based on a novel AAV gene therapy technology with which there is limited clinical experience to date, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

Our product candidates are based on gene therapy technology and our future success depends on the successful development of this novel therapeutic approach. There can be no assurance that any development problems we or other gene therapy companies experience in the future related to gene therapy technology will not cause significant delays or unanticipated costs in the development of our product candidates, or that such development problems can be solved. In addition, the clinical trial requirements of the FDA, EMA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied therapeutic modalities. Further, as we are developing novel treatments for diseases in which there is limited clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, EMA or comparable foreign regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. To date, only one gene therapy product has been approved in the United States and only two gene therapy products have been approved in Europe, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the European Union, or EU, or other jurisdictions. Further, approvals by one regulatory agency may not be indicative of what other regulatory agencies may require for approval.

Regulatory requirements governing gene therapy products have evolved and may continue to change in the future. For example, in July 2018, the FDA issued a number of draft and final guidance documents for the industry to describe the FDA's current thinking with regard to the regulatory framework for gene therapy development, including guidance related to chemistry, manufacturing, and controls, or CMC, information and clinical trial design parameters to support product registration. These and other requirements and guidelines promulgated by FDA and other regulatory review agencies, committees and advisory groups may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions.

The FDA, the National Institutes of Health, or NIH, the EMA and other regulatory agencies have demonstrated caution in their regulation of gene therapy treatments, and ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of our product candidates, which may be difficult to predict.

The FDA, NIH, other regulatory agencies at both the federal and state level in the United States, U.S. congressional committees, and the EMA and other foreign governments, have expressed interest in further regulating the biotechnology industry, including gene therapy and genetic testing. For example, the EMA advocates a risk-based approach to the development of a gene therapy product. Any such further regulation may delay or prevent commercialization of some or all of our product candidates. For example, in 1999, a patient died during a gene therapy clinical trial that utilized an adenovirus vector and it was later discovered that adenoviruses could generate an extreme immune system reaction that can be life-threatening. In January 2000, the FDA halted that trial and began investigating 69 other gene therapy trials underway in the United States, 13 of which required remedial action. In 2003, the FDA suspended 27 additional gene therapy trials involving several hundred patients after learning that some patients treated in a clinical trial in France had subsequently developed leukemia. While the new AAV vectors that we use across our portfolio of product candidates have been developed to reduce these side effects, gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop.

Regulatory requirements in the United States and abroad governing gene therapy products have changed frequently and may continue to change in the future. Our planned clinical trials may be subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or RAC, even though none have been required to date. As of April 2016, the new NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, including gene therapy, provide the opportunity for one or more oversight bodies (IRB or the Institutional Biosafety Committee, or IBC) to request a public RAC review based on their own review of the protocol and NIH requirements. Regardless of the request for public review, NIH makes its own assessment as to whether the protocol would significantly benefit from a public RAC review. The NIH's recommendations are shared with the FDA and the oversight bodies. The RAC can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and has not objected to its initiation or has notified the sponsor that the study may begin. Conversely, the FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or has

recommended against an in-depth, public review. If there is a public RAC review, the receipt of the final recommendation letter concludes the protocol registration process and then oversight body approval can be issued. 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 product candidates. Similarly, the EMA governs the development of gene therapies in the EU and may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. As we advance our 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 such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate and the approval may be for a narrower indication than we seek.

Prior to commercialization, our product candidates must be approved by the FDA pursuant to a BLA in the United States and by the EMA and similar regulatory authorities outside the United States. The process of obtaining marketing approvals, both in the United States and abroad, is expensive and takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have no experience in submitting and supporting the applications necessary to gain marketing approvals, and, in the event regulatory authorities indicate that we may submit such applications, we may be unable to do so as quickly and efficiently as desired. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical studies or clinical trials. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate.

Approval of our product candidates may be delayed or refused for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical programs or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- our manufacturing facilities, or those of third-party manufacturers with which we contract or procure certain services or raw materials, may not be adequate to support approval of our product candidates; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or REMS. These regulatory authorities may require precautions or contra-indications with respect to conditions of use or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially and adversely affect our business, financial condition, results of operations and prospects.

Further, the regulatory authorities may require concurrent approval or the CE mark, indicating conformity with applicable European Community directives, of a companion diagnostic device. For the product candidates we currently are developing, we believe that diagnoses based on symptoms, in conjunction with existing genetic tests developed and administered by laboratories certified under the Clinical Laboratory Improvement Amendments, are sufficient to diagnose patients and will be permitted by the FDA. For future product candidates, however, it may be necessary to use FDA-cleared or FDA-approved diagnostic tests to diagnose patients or to assure the safe and effective use of product candidates in trial subjects. The FDA refers to such tests as *in vitro* companion diagnostic devices. In August 2014, the FDA issued a final guidance document describing the agency's current thinking about the development and regulation of *in vitro* companion diagnostic devices. The final guidance articulates a policy position that, when an *in vitro* diagnostic device is essential to the safe and effective use of a therapeutic product, the FDA generally will require approval or clearance of the diagnostic device at the same time that the FDA approves the therapeutic product. At this point, it is unclear how the FDA will apply this policy to our current or future gene therapy product candidates. Should the FDA deem genetic tests used for diagnosing patients for our therapies to be *in vitro* companion diagnostics requiring FDA clearance or approval, we may face significant delays or obstacles in obtaining approval of a BLA for our product candidates. In the EU, the European Commission has proposed substantial revisions to the current regulations governing *in vitro* diagnostic medical devices. If adopted in their current form, these revisions may impose additional obligations on us that may impact the development and authorization of our product candidates in the EU.

We may never obtain FDA approval for any of our product candidates in the United States, and even if we do, we may never obtain approval for or commercialize any of our product candidates in any other jurisdiction, which would limit our ability to realize their full market potential.

In order to eventually market any of our product candidates in any particular foreign jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a jurisdiction-by-jurisdiction basis regarding safety and efficacy. Approval by the FDA in the United States, if obtained, 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 preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any product candidates approved for sale in any jurisdiction, including 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 our products will be unrealized.

Delays or disruptions in our manufacturing process development and operations may delay or disrupt our development and commercialization efforts.

We have invested in our own state-of-the-art cGMP manufacturing facility in South San Francisco, California, where we are developing and implementing novel production technologies to supply our preclinical studies and clinical trials. We believe that development of an internal manufacturing capability provides us with enhanced control of material supply for preclinical studies and clinical trials and commercial markets, enables the more rapid implementation of process changes and allows for better control over manufacturing-associated expenses and intellectual property. However, we have limited experience as a company in developing a manufacturing facility and there exist only a small number of CMOs with the experience necessary to

manufacture our product candidates. We may have difficulty hiring experts to staff and operate our internal manufacturing facility or finding and maintaining relationships with external CMOs and, accordingly, our production capacity could be limited. Even if we are successful, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, lack of capacity, delays in implementation of novel in-house technologies or scale-up activities, labor shortages, natural disasters, including earthquakes, power failures and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy. The occurrence of any of these factors could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Before we may initiate a clinical trial of our product candidates, we must demonstrate to the FDA that the CMC for our product candidates meets applicable requirements, and in the EU, a manufacturing authorization must be obtained from the appropriate EU regulatory authorities. In addition, we must pass a pre-approval inspection of our manufacturing facility by the FDA before any of our product candidates can obtain marketing approval. In order to obtain approval, we will need to ensure that all of our processes, methods and equipment are compliant with cGMPs and other regulations, and perform extensive audits of vendors, contract laboratories and suppliers. If we or any of our vendors, contract laboratories or suppliers is found to be out of compliance with cGMPs or other regulations, we may experience delays or disruptions in manufacturing while we work to remedy the noncompliance, or while we work to identify suitable replacement vendors. If we or our CMOs are unable to reliably produce products to specifications acceptable to the FDA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CMOs will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. Any of these challenges could delay initiation of, or completion of, clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods and have an adverse effect on our business, financial condition, results of operations and growth prospects.

We may not be successful in our efforts to build a pipeline of additional product candidates.

Our business model is centered on applying our AAV gene therapy technology platform and expertise in rare neuromuscular diseases to develop and advance a broad portfolio of gene therapy product candidates across multiple modalities through development into commercialization. We may not be able to identify and develop new product candidates, and even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not receive regulatory approval. For example, during preclinical or clinical development, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

Our product candidates based on gene therapy technology may cause undesirable and unforeseen side effects or be perceived by the public as unsafe, which could delay or prevent their advancement into clinical trials or regulatory approval, limit the commercial potential or result in significant negative consequences.

There have been several significant adverse side effects in prior clinical trials of gene therapy product candidates, including reported cases of leukemia and death seen in other trials using other vectors. While the newer AAV vectors that we use have been developed to reduce these side effects, AAV gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. 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.

Known side effects of treatment with gene therapy products include an immunologic reaction early after administration that could be detrimental to the patient's health or substantially limit the effectiveness and durability of the treatment, including the development of a T-cell-mediated immunological response, most often seen affecting the liver. In ASPIRO, our Phase 1/2 clinical trial of AT132, we have seen several adverse events, or SAEs, that were deemed to be probably or possibly related to treatment, including elevations of liver enzymes, a signal that a T-cell mediated immune response has likely occurred. At our May 2019 ASPIRO update, we reported a series of adverse events that were deemed to be SAEs. These included troponin I elevations, creatine kinase elevations, myocarditis, ST segment elevation, atrial tachycardia, hyperbilirubinemia, nausea, vomiting and fever. To date, all of the reported adverse events in ASPIRO have resolved without treatment or been controlled by treatment. However, if we are unable to clinically manage potential safety events in the future, we may decide or be required to halt or delay further clinical development of our product candidates.

In addition to side effects caused by a product candidate, the administration process or related procedures also can cause adverse side effects. If any such adverse events occur, our clinical trials could be suspended or terminated. If we are unable to

demonstrate that any adverse events were caused by the administration process or related procedures, the FDA, the European Commission, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Even if we can demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to not initiate, delay, suspend or terminate any future clinical trial of any of our product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly.

Additionally, if any of our product candidates receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of the product outweigh its risks, which may include, among other things, a Medication Guide outlining the risks of the product for distribution to patients and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by any of our products, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label of such product;
- we may be required to change the way such a product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these occurrences may harm our business, financial condition and prospects significantly.

The diseases we seek to treat have low prevalence and it may be difficult to identify patients with these diseases, which may lead to delays in enrollment for our trials or slower commercial revenue if approved.

Genetic diseases generally, and especially those that our product candidates are designed to address, have low rates of incidence and prevalence. For example, we estimate that the incidence of XLMTM is approximately one in 40,000 to one in 50,000 male births, the incidence of Pompe disease is approximately one in 40,000 births, the incidence of DM1 is approximately one in 8,000 births, and the incidence of DMD is approximately one in 3,500 to one in 5,000 male births. In addition, as we pursue increasingly precise forms of genetic medicines, the number of patients we can treat with a single product candidate may be less than the estimated patient population. For example, we estimate that AT702, our lead product candidate in DMD, may be able to treat up to approximately 6% of DMD patients that have genotypes amenable to exon 2 skipping or with mutations in exons 1-5 of the dystrophin gene. To address patients amenable to exon 51 and 53 skipping, we are developing separate product candidates, AT751 and AT753, respectively. In combination, these three product candidates may be able to treat up to approximately 25% of DMD patients, and we would need to develop additional product candidates to treat other mutations utilizing our vectorized exon skipping approach. In total, we estimate that up to 80% of DMD patients may have genotypes amenable to exon skipping approaches. In addition, some of our potential patients may have neutralizing antibodies to the AAV capsid serotypes we employ, which may limit our ability to treat them, or affect the therapeutic efficacy of our product candidates once administered. Working in rare genetic diseases poses unique challenges versus more conventional drug development for primary care markets, including the timely recruitment and enrollment of a sufficient number of eligible patients into clinical trials. Further, because newborn screening for certain of the diseases that our product candidates are designed to address is not widely adopted, and it can be difficult to diagnose these diseases in the absence of a genetic screen, we may have difficulty finding patients who are eligible to participate in our trials. Patient enrollment into clinical trials may be affected by other factors including:

- the ability to identify and recruit patients that meet study eligibility and exclusion criteria;
- the severity of the disease under investigation;
- design of the study protocol;
- the perceived risks, benefits and convenience of administration of the product candidate being studied;
- our efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians; and
- the proximity and availability of clinical trial sites to prospective patients.

Our inability to enroll a sufficient number of patients for our planned clinical trials would result in significant delays and could require us to not initiate or abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result

in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Additionally, our projections of the number of patients living with the rare diseases our product candidates are designed to address, as well as the subset of those patients who have the potential to benefit from our product candidates, are based on estimates. The total addressable market opportunity for our product candidates will ultimately depend upon, among other things, the final labeling for each of our product candidates, if our product candidates are approved for sale in our target indications, acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients globally may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. Our product candidates may potentially be dosed on a one-time basis, which means that patients who enroll in our clinical trials may not be eligible to receive our product candidates on a commercial basis if they are approved, leading to lower revenue potential.

A Regenerative Medicine Advanced Therapy (RMAT) Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

Established under the 21st Century Cures Act, the RMAT designation is an expedited program for the advancement and approval of regenerative medicine products where preliminary clinical evidence indicates the potential to address unmet medical needs for life-threatening diseases or conditions. We have received RMAT designation for our AT132 program and plan to seek RMAT designation for our other product candidates if the preliminary clinical data support such designation. Similar to Breakthrough Therapy designation, the RMAT designation allows companies developing regenerative medicine therapies to work more closely and frequently with the FDA, and RMAT-designated products may be eligible for priority review and accelerated approval. In a November 2017 draft guidance document, the FDA stated that gene therapies, including genetically modified cells, that lead to a durable modification of cells or tissues, may meet the definition of a regenerative medicine therapy. For product candidates that have received a RMAT designation, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

RMAT designation is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for RMAT designation, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of RMAT designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as RMAT therapies, the FDA may later decide that the product no longer meets the conditions for qualification.

A Fast Track Designation by the FDA, or a Priority Medicines (PRIME) designation by the EMA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

We have received Fast Track Designation for AT132, and in the future, we may seek additional Fast Track Designations for other product candidates. If a drug or biologic, in our case, is intended for the treatment of a serious or life-threatening condition and the biologic demonstrates the potential to address unmet medical needs for this condition, the biologic sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether to grant this designation. Even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many biologics that have received Fast Track Designation have failed to obtain approval.

We may also seek accelerated approval for products that have obtained Fast Track Designation. Under the FDA's accelerated approval program, the FDA may approve a biologic for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. For biologics granted accelerated approval, post-marketing confirmatory trials are required to describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence and, in some cases, the FDA may require that the trial be designed and/or initiated prior to approval. Moreover, the FDA may withdraw approval of any product candidate or indication approved under the accelerated approval pathway if, for example:

- the trial or trials required to verify the predicted clinical benefit of the product candidate fail to verify such benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the biologic;
- other evidence demonstrates that the product candidate is not shown to be safe or effective under the conditions of use;
- we fail to conduct any required post-approval trial of the product candidate with due diligence; or
- we disseminate false or misleading promotional materials relating to the product candidate.

In addition to the FDA's Fast Track and RMAT Designations, other regulatory authorities may grant their own priority designations, including the Priority Medicines, or PRIME, designation granted by the EMA. We have received PRIME designation for AT132 and in the future, we may seek additional PRIME designations for other product candidates. PRIME designation is subject to risks and uncertainties similar to those described above for Fast Track and RMAT Designations, and our product candidates which have received PRIME designation may not experience a faster development process, review or approval compared to conventional EMA procedures.

We may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity, for our product candidates, and may be unsuccessful in obtaining Orphan Drug Designation or transfer of designations obtained by others for future product candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs, or biologics in our case, intended to treat relatively small patient populations as orphan drugs. Under the U.S. Orphan Drug Act, the FDA may designate a biologic as an orphan drug if it is intended to treat a rare disease or condition, which is defined as a patient population of fewer than 200,000 individuals in the United States. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits for qualified clinical research costs, and prescription drug user fee waivers. Similarly, in the EU, the European Commission grants Orphan Drug Designation after receiving the opinion of the EMA's Committee for Orphan Medicinal Products on an Orphan Drug Designation application. In the EU, Orphan Drug Designation is intended to promote the development of biologics that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the EU and for which no satisfactory method of diagnosis, prevention or treatment has been authorized (or the product would be a significant benefit to those affected). In the EU, Orphan Drug Designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a biologic with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the biologic is entitled to a period of marketing exclusivity, which precludes EMA or the FDA from approving another marketing application for the same biologic and indication for that time period, except in limited circumstances. If our competitors are able to obtain orphan drug exclusivity prior to us for products that constitute the same active moiety and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time. The applicable period is seven years in the United States and ten years in the EU. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for Orphan Drug Designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

As part of our business strategy, we have sought and received Orphan Drug Designation for AT132 in the United States and Europe. Both the FDA and EMA have granted orphan drug designation to a prototype version of AT845, which we plan to update to reflect the final construct we intend to advance into clinical trials. However, Orphan Drug Designation does not guarantee future orphan drug marketing exclusivity.

Additionally, even if we obtain orphan drug exclusivity for our product candidates, that exclusivity may not provide effective protection from competition because drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA can also subsequently approve a later application for the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

A Rare Pediatric Disease designation by the FDA does not guarantee that the NDA or BLA for the product will qualify for a priority review voucher upon approval, and it does not lead to a faster development or regulatory review process, or increase the likelihood that any of our product candidates will receive marketing approval.

Under the Rare Pediatric Disease Priority Review Voucher program, upon the approval of a qualifying BLA or new drug application, or NDA, for the treatment of a rare pediatric disease, the sponsor of such an application would be eligible for a rare pediatric disease priority review voucher that can be used to obtain priority review for a subsequent BLA or NDA. In July 2017, the FDA notified us that we obtained a Rare Pediatric Disease designation for AT132 for the treatment of XLMTM. If a product candidate is designated before October 1, 2020, as is the case with AT132, it is eligible to receive a voucher if it is approved before October 1, 2022. However, there is no guarantee that any of our product candidates will be approved by that date, or at all, and, therefore, we may not be in a position to obtain priority review vouchers prior to expiration of the program, unless Congress further reauthorizes the program. Additionally, designation of a drug for a rare pediatric disease does not guarantee that a BLA will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Finally, a Rare Pediatric Disease designation does not lead to faster development or regulatory review of the product, or increase the likelihood that it will receive marketing approval.

We rely on third parties to conduct our preclinical studies and clinical trials, and rely on them to perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

Although we have recruited a team that has experience with clinical trials, as a company we have limited experience in conducting clinical trials. Moreover, we do not have the ability to independently conduct preclinical studies and clinical trials, and we have relied upon, and plan to continue to rely upon medical institutions, clinical investigators, contract laboratories and other third parties, or our CROs, to conduct preclinical studies and clinical trials for our product candidates. We expect to rely heavily on these parties for execution of preclinical studies and clinical trials for our product candidates and control only certain aspects of their activities. Nevertheless, we will be responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards and our reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our preclinical studies and clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

We and our CROs will be required to comply with regulations, including GCPs for conducting, monitoring, recording and reporting the results of preclinical studies and clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any drugs in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that, upon inspection, the FDA will determine that any of our future clinical trials will comply with GCPs. In addition, our clinical trials must be conducted with product candidates produced in accordance with the requirements of cGMP regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action.

Although we intend to design our planned clinical trials for our product candidates, for the foreseeable future CROs will conduct all of our planned clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct preclinical studies and clinical trials will also result in less day-to-day control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any preclinical studies or clinical trials with which such CROs are associated with may be extended, delayed or terminated. In such cases, we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates in the subject indication could be harmed, our costs could increase and our ability to generate revenue could be delayed.

Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Our product candidates and the activities associated with their development and potential commercialization, including their testing, manufacture, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, compliance with cGMPs, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, including periodic inspections by the FDA and other regulatory authorities, and requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of any approved product. The FDA closely regulates the post-approval marketing and promotion of drugs and biologics to ensure drugs and biologics are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products. If we promote our product candidates beyond their potentially approved indications, we may be subject to enforcement action for off-label promotion. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

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

- restrictions on such product candidates, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of any approved product from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of product candidates;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our product candidates;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with U.S., European and other requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with U.S., European and other governmental requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our product candidates for which we intend to seek approval may face competition from biosimilars sooner than anticipated.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, an abbreviated pathway for the approval of biosimilar and interchangeable biological products was created. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as interchangeable based on its similarity to an existing reference product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product is approved under a BLA. To date a handful of biosimilar products and no interchangeable products have been approved under the BPCIA. However, the law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning

are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that if any of our product candidates are approved as a biological product under a BLA, it should qualify for the 12-year period of exclusivity. However, there is a risk that the FDA will not consider any of our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Additionally, this period of regulatory exclusivity does not apply to companies pursuing regulatory approval via their own traditional BLA, rather than via the abbreviated pathway. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. Finally, there has been public discussion of potentially decreasing the period of exclusivity from the current 12 years. If such a change were to be enacted, our product candidates, if approved, could have a shorter period of exclusivity than anticipated.

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

In the United States 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 of 2010, or collectively the ACA, 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 current federal administration has indicated an intent to repeal the ACA. The President has indicated an intent to address prescription drug pricing and recent Congressional hearings have brought increased public attention to the costs of prescription drugs. These actions and the uncertainty about the future of the ACA and healthcare laws may put downward pressure on pharmaceutical pricing and increase our regulatory burdens and operating costs.

Moreover, the Drug Supply Chain Security Act imposes new obligations on manufacturers of pharmaceutical products related to product tracking and tracing. 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, or whether the current regulations, guidance or interpretations will be changed, or what the impact of such changes on our business, if any, may be.

The insurance coverage and reimbursement status of newly-approved gene therapy products is uncertain. We may not be able to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved.

It is difficult to predict what third-party payors will decide with respect to coverage and reimbursement for our product candidates, as gene and cell therapies are novel products that are generally anticipated to establish premium pricing and are initially intended as a one-time single administration. In the United States, there has been a small number of gene and cell therapy products approved for marketing by the FDA (all in 2017). While there is no body of established pricing and reimbursement practices for these novel gene and cell therapy products, and no uniform policy of coverage and reimbursement exists among third-party payors, these products may establish a pricing and reimbursement precedent for our product candidates, if approved. The Centers for Medicare and Medicaid Services, or CMS, administers the Medicare and Medicaid programs, which are increasingly used as models for how private payors develop their coverage and reimbursement policies, but coverage and reimbursement for products can differ significantly from payor to payor. It is difficult to predict what the CMS will decide with respect to coverage and reimbursement for a fundamentally novel gene therapy product such as ours, or how the CMS's decision will affect our ability to obtain coverage and adequate reimbursement from other third-party payors, if any of our product candidates receive FDA approval. Moreover, reimbursement agencies in the European Union may be more conservative than the CMS. For example, several cancer drugs have been approved for reimbursement in the United States but have not been approved for reimbursement in certain European Union Member States.

Our operations and relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties including criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with providers, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the

business or financial arrangements and relationships through which we market, sell and distribute any product candidates for which we obtain marketing approval.

Restrictions under applicable U.S. federal and state healthcare laws and regulations may include the following:

- 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 either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- federal false claims laws, including the federal False Claims Act, imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or 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 statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health, or HITECH Act, and its implementing regulations, also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report payments and other transfers of value to physicians and teaching hospitals, as well as certain ownership and investment interests held by physicians and their immediate family, which includes annual data collection and reporting obligations; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern 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 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 may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of product candidates from government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

Risks Related to Manufacturing and Commercialization

Gene therapy products are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in our development or commercialization programs or otherwise harm our business.

The manufacturing processes used to produce our product candidates are complex, novel and have not been validated for commercial use. Several factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, disruption in utility services, human error, disruptions in the operations of our suppliers, or natural disasters. We currently manufacture all of our preclinical study and clinical trial material at our internal cGMP manufacturing plant located in South San Francisco, and, if approved, we plan to manufacture the commercial supply of AT132 at this same facility. We do not currently have redundant manufacturing capabilities, and if we encounter any production interruptions at our facility, it could be detrimental to our ability to conduct ongoing operations and otherwise harm our business, financial condition, results of operations and business prospects.

Our product candidates require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of biologics 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 is consistent from lot-to-lot or will perform in the intended manner. Accordingly, we employ multiple steps to control the manufacturing process to assure that the process works reproducibly and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, 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 to conduct clinical trials or supply commercial markets. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet the FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other foreign 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, the EMA or other foreign 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. 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.

We also may encounter problems hiring and retaining the experienced scientific, quality assurance, quality-control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing process or facilities could result in delays in our planned clinical trials and increased costs, and could make us a less attractive collaborator for potential partners, including larger biotechnology and pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in our manufacturing process could restrict our ability to meet potential future market demand for our products.

We and our collaborators, third-party manufacturers and suppliers use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and our collaborators, third-party manufacturers and suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Any contamination in our or our third parties' manufacturing process, shortages of raw materials or reagents or failure of any of our key suppliers to deliver necessary components of our platform 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 materially adversely affect our or our third-party vendors' ability to produce our gene therapies on schedule and could therefore harm our results of operations and cause reputational damage.

The raw materials required in our and our third-party vendor manufacturing processes are derived from biological sources. There can be no assurance that we or our third-party vendors have, or will be able to obtain on commercially reasonable terms, or at all, sufficient rights to these materials derived from biological sources. Such raw materials are difficult to procure and may also 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 adversely impact or disrupt the clinical and commercial manufacturing of our product candidates, which could materially and adversely affect our operating results and development timelines.

We rely on third-party suppliers for the supply and manufacture of certain components of our technology. Should our ability to procure these material components from our suppliers be compromised, our ability to continuously operate would be

impaired until an alternative supplier is sourced, qualified and tested, which could limit our ability to produce the necessary clinical and commercial supply of our product candidates and harm our business.

We do not have complete control over any current or future third-party manufacturers' processes and compliance with applicable regulations.

Despite having our own internal cGMP manufacturing capability, we may at times utilize third-party manufacturers to increase our manufacturing capacity or for redundancy purposes. Third-party manufacturers may not have the experience or ability to produce our product candidates at clinical or commercial scales within our planned timeframe and cost parameters, and such manufacturers may run into technical or scientific issues that we may be unable to resolve in a timely manner or with available funds.

Additionally, the manufacturing of product candidates for clinical and commercial purposes must comply with the cGMP and other relevant regulatory requirements. The cGMP requirements govern quality control and documentation policies and procedures. Third-party manufacturers must demonstrate to the FDA that they can make the product candidate in accordance with the cGMP requirements as part of a pre-approval inspection prior to FDA approval of the product candidate. Failure to pass a pre-approval inspection might significantly delay FDA approval of our product candidates. If any third-party manufacturer fails to comply with FDA or applicable foreign regulatory requirements, we would be subject to possible regulatory action, which could limit the jurisdictions in which we are permitted to sell our products. As a result, our business, financial condition and results of operations may be materially harmed.

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Ethical, social and legal concerns about gene therapy could result in additional regulations restricting or prohibiting our products. Even with the requisite approvals from FDA in the United States, the EMA in the EU and other regulatory authorities internationally, the commercial success of our product candidates will depend, in part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of gene therapy products and, in particular, our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by the FDA, EMA or other regulatory authorities;
- the willingness of physicians to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party payor coverage and adequate reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be fully known until after it is launched.

We face significant competition in an environment of rapid technological change and it is possible that our competitors may achieve regulatory approval before us or develop therapies that are more advanced or effective than ours, which may harm our business and financial condition, and our ability to successfully market or commercialize our product candidates.

The biotechnology and pharmaceutical industries, including the gene therapy field, are characterized by rapidly changing technologies, competition and a strong emphasis on intellectual property. We are aware of several companies focused on developing gene therapies in various indications as well as several companies addressing other methods for modifying genes and regulating gene expression. We may also face competition from large and specialty biotechnology and pharmaceutical companies, academic research institutions, government agencies and public and private research institutions. To our knowledge, other therapies, products or product candidates currently in development include:

For the treatment of XLMTM, Valerion Therapeutics, LLC, or Valerion, is studying VAL-0620, a fusion protein consisting of an antibody linked to MTM1. Preclinical evaluation of this approach in the MTM1 murine model demonstrated improvements in both muscle structure and function, as reported in a 2013 publication. Working in collaboration with IONIS Pharmaceuticals, Inc., or Ionis, Dynacure S.A.S., or Dynacure, is studying Dyn101, an antisense oligonucleotide designed to downregulate the expression of the DNM2 protein as a potential treatment for centronuclear myopathies. Preclinical evaluation of this approach in a MTM1 knockout mouse model demonstrated a reduction of DNM2 protein expression in muscle, correction of muscle pathology and extended lifespan of affected mice. Neither the Valerion or Dynacure programs have been reported to have progressed to clinical development.

For the treatment of Pompe disease, the current standard of care is enzyme replacement therapy (ERT) with recombinant GAA protein. Genzyme Corporation, or Genzyme, currently markets MYOZYME and LUMIZYME, which are ERTs for the treatment of Pompe disease. Multiple companies, including Genzyme, Amicus Therapeutics, Inc., or Amicus, Valerion and Oxyrane UK Limited, are currently reported to be developing next generation ERT to treat Pompe disease. The furthest advanced of these is neoGAA from Genzyme. In addition, there are currently six companies researching alternative gene therapy approaches to treating Pompe disease, including Spark Therapeutics, Inc., AVROBIO, Inc., Lacerta Therapeutics, Inc., Regeneron Pharmaceuticals, Inc., Amicus and Actus Therapeutics, Inc., or Actus. Of these, only Actus has reported the initiation of a Phase 1/2 human clinical trial.

For the treatment of DMD, there are several genetic medicines approaches being pursued. Sarepta Therapeutics, Inc., or Sarepta, has been evaluating multiple technologies, including naked antisense oligonucleotide, or ASO, therapies, and has received approval of Exondys51 (eteplirsen) for patients with DMD genotypes amenable to exon 51 skipping. Sarepta has other exon skipping product candidates in development, including one for exon 53 skipping for which an NDA has been filed, one for exon 45 skipping which has been reported to be in phase 3 development, and one for exon 52 skipping which has been reported to be in preclinical development. Sarepta, Pfizer Inc., and Solid Biosciences, Inc. are each in clinical development with AAV-based microdystrophin gene replacement product candidates. Sarepta is also pursuing a surrogate gene therapy program, overexpressing the GALGT2 gene, and is in early clinical development. Exonics Therapeutics, Inc. and Editas Medicine, Inc. are in preclinical development with CRISPR/Cas 9 gene editing approaches to DMD. Wave Life Sciences, Inc., or Wave Life Sciences, is reported to be in a Phase 1/2 trial with an exon skipping approach utilizing stereopure ASOs. Wave Life Sciences has reported pursuing product candidates to skip exons 51, 55, 53, 45, 44 and 52.

For DM1, there is no currently approved disease modifying therapy, and patients are frequently treated with different drugs to address certain symptoms of the disease. AMO-Pharma, Ltd. has reported that it has completed a Phase 2 study in patients with congenital and childhood DM1 with Tideglusib (AMO-02), a glycogen synthase kinase 3 beta enzyme inhibitor that influences CUGBP1 activity. Several companies and academic institutions have also reported programs in DM1, but none have yet progressed to clinical trials. These include Wave Life Sciences and Ionis that are pursuing antisense oligonucleotide-based technologies, Genethon, and Locana, Inc. that are pursuing gene/RNA editing technologies, Expansion Therapeutics, Inc. that is pursuing a CUG-repeat targeting small molecule, and Dyne Therapeutics Inc. that is pursuing an antibody-targeted oligonucleotide therapy.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources than we do, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any product candidates that we may develop. 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, if ever. Additionally, new or advanced technologies developed by our competitors may render our current or future product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities can include completing preclinical studies and initiating and completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products that are approved and satisfying any post marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause investors to lose all or part of their investment.

The pricing, insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

Our target indications have small patient populations. In order for products that are designed to treat smaller patient populations to be commercially viable, the reimbursement for such products must be higher, on a relative basis, to account for the lack of volume. Accordingly, we will need to implement a coverage and reimbursement strategy for any approved product candidate that accounts for the smaller potential market size. If we are unable to establish or sustain coverage and adequate reimbursement for any future product candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved.

We expect the price for a single administration of gene therapy products, such as those we are developing, to be substantial when and if they achieve regulatory approval. Therefore, we expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of any of our product candidates will depend substantially, both domestically and internationally, on the extent to which the price for our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers and other third-party payors. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement by government authorities for new products are typically made by CMS, since CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. However, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Further, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. It is difficult to predict what CMS will decide with respect to reimbursement for novel products such as ours since there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the EU, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, the prices of products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be less than in the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third-party payors, in the United States and internationally, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of certain third-party payors, such as health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the

healthcare market. Recently there have been instances in which third-party payors have refused to reimburse treatments for patients for whom the treatment is indicated in the FDA-approved product label. Even if we are successful in obtaining FDA approvals to commercialize our products, we cannot guarantee that we will be able to secure reimbursement for all patients for whom treatment with our products is indicated.

In addition to CMS and private payors, professional organizations such as the American Medical Association, or the AMA, can influence decisions about reimbursement for new products by determining standards for care. In addition, many private payors contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our product candidates. Even if favorable coverage and reimbursement status is attained for one or more products for which we or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

If we are unable in the future to establish U.S. or global sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if they are approved and we may not be able to generate any revenue.

We currently do not have a marketing or sales team for the marketing, sales and distribution of any of our product candidates that are able to obtain regulatory approval. To commercialize any product candidates after approval, we must build on a territory-by-territory basis marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If our product candidates receive regulatory approval, we may decide to establish an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates, which will be expensive and time-consuming and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of any of our product candidates that we obtain approval to market.

With respect to the commercialization of all or certain of our product candidates, we may choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements when needed on acceptable terms, or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval or any such commercialization may experience delays or limitations. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We may not be successful in finding strategic collaborators for continuing development of certain of our product candidates or successfully commercializing or competing in the market for certain indications.

We have in the past, and may in the future, decide to collaborate with non-profit organizations, universities, and pharmaceutical and biotechnology companies for the development and potential commercialization of existing and new product candidates. We face significant competition in seeking appropriate collaborators. Whether we 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. 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 drugs, 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. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may 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 may not be able to further develop our product candidates or bring them to market and generate product revenue.

The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

Risks Related to Our Financial Position

Comprehensive tax reform bills could increase the tax burden on our orphan drug programs and adversely affect our business and financial condition.

In December 2017, the U.S. government enacted comprehensive tax legislation that includes significant changes to the taxation of business entities. These changes include, among others, (i) a permanent reduction to the corporate income tax rate, (ii) a partial limitation on the deductibility of business interest expense, (iii) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a territorial system (along with certain rules designed to prevent erosion of the U.S. income tax base) and (iv) a one-time tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate.

Further, the recently enacted comprehensive tax legislation, among other things, reduces the orphan drug tax credit from 50% to 25% of qualifying expenditures. When and if we become profitable, this reduction in tax credits may result in an increased federal income tax burden on our orphan drug programs as it may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and, despite being partially off-set by a reduction in the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, may increase our total federal tax liability attributable to such programs.

Notwithstanding the reduction in the corporate income tax rate, the overall impact of this tax reform is uncertain, and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the recently enacted federal tax law.

We have a history of operating losses, and we may not achieve or sustain profitability. We anticipate that we will continue to incur losses for the foreseeable future. If we fail to obtain additional funding to conduct our planned research and development efforts, we could be forced to delay, reduce or eliminate our product development programs or commercial development efforts.

We are an early-stage biotechnology company with a limited operating history on which investors may base their investment decision. Biotechnology product development is a highly speculative undertaking and involves a substantial degree of risk. Our operations to date have been limited primarily to organizing and staffing our company, business planning, raising capital, acquiring and developing product and technology rights, manufacturing, and conducting research and development activities for our product candidates. We have never generated any revenue from product sales. We have not obtained regulatory

approvals for any of our product candidates, and have funded our operations to date through proceeds from sales of our preferred stock and common stock.

We have incurred net losses in each year since our inception. We incurred a net loss of $49.4 million for the three months ended March 31, 2019 and net losses of $128.8 million and $90.2 million for the years ended December 31, 2018 and 2017, respectively. As of March 31, 2019, we had an accumulated deficit of $368.9 million. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future as we intend to continue to conduct research and development, clinical testing, regulatory compliance activities, manufacturing activities, and, if any of our product candidates is approved, sales and marketing activities, together with anticipated general and administrative expenses for all of the foregoing. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital.

We expect that we will need to raise additional funding before we can expect to become profitable from any potential future sales of our products. This additional financing may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit, or terminate our product development efforts or other operations.

We will require substantial future capital in order to complete planned and future preclinical and clinical development of our current and future product candidates, if any, and potentially commercialize these product candidates. We expect our spending levels to increase in connection with our preclinical studies and clinical trials of our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant expenses related to commercial launch, product sales, medical affairs, marketing, manufacturing and distribution. Furthermore, we expect to incur additional costs associated with expanding staff and operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our licensing activities, our research and development programs or other operations.

Our operations have consumed significant amounts of cash since inception. As of March 31, 2019, our cash, cash equivalents and marketable securities were $375.0 million, which includes short-term investments of $236.3 million and long-term investments of $5.5 million.

Our future capital requirements will depend on many factors, including:

- the costs associated with the scope, progress and results of discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the costs associated with the development of our internal manufacturing facility and processes;
- the costs related to the extent to which we enter into partnerships or other arrangements with third parties in order to further develop our product candidates;
- the costs and fees associated with the discovery, acquisition or in-license of product candidates or technologies;
- our ability to establish collaborations on favorable terms, if at all;
- the costs of future commercialization activities, if any, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of product candidates that we do not expect to be commercially available for many years, if at all. Accordingly, to achieve our business objectives, we will need to continue to rely on additional financing, which may not be available to us on acceptable terms, or at all.

Our ability to utilize our net operating loss carryforwards may be subject to limitation.

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. As of December 31, 2018, we had federal net operating loss carryforwards of $265.5 million, which begin to expire in 2033. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset

future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Risks Related to Intellectual Property

If we are unable to obtain and maintain patent protection for our products and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our products and technology may be adversely affected.

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other countries for our product candidates and future products, as well as our core technologies, including our manufacturing know-how. We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business by seeking, maintaining and defending our intellectual property, whether developed internally or licensed from third parties. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of gene therapy. Additionally, we intend to rely on regulatory protection afforded through rare drug designations, data exclusivity and market exclusivity as well as patent term extensions, where available.

Our in-licensed patents and patent applications are directed to the compositions of matter and methods of use related to various aspects of our product candidates as well as certain aspects of our manufacturing capabilities. 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.

The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our licensed patents have, or that any of our pending licensed patent applications that mature into issued patents will include, claims with a scope sufficient to protect our current and future product candidates or otherwise provide any competitive advantage. For example, we have licensed certain intellectual property rights from Genethon, and the Genethon patent families were filed only in the United States, and therefore these patent families will not provide patent protection outside the United States. While other patent families include foreign counterparts, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally twenty years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. 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. If any of our product candidates are approved by the FDA as a biological product under a BLA in the United States, we believe the product would qualify for a 12-year period of exclusivity. Moreover, our exclusive licenses are subject to retained rights, which may adversely impact our competitive position. As a result, our licensed patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar to our product candidates, including biosimilar versions of such products. In addition, the patent portfolio licensed to us is, or may be, licensed to third parties, such as outside our field, and such third parties may have certain enforcement rights. Thus, patents licensed to us could be put at risk of being invalidated or interpreted narrowly in litigation filed by or against another licensee or in administrative proceedings brought by or against another licensee in response to such litigation or for other reasons.

Other parties have developed technologies that may be related or competitive to our own and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and in 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 the inventors of our licensed patents and applications were the first to make the inventions claimed in those patents or pending patent applications, or that they were the first to file for patent protection of such inventions. Further, there can be no assurance that all of the potentially relevant prior art relating to our licensed patents and patent applications has been found. If such prior art exists, it can invalidate a

patent or prevent a patent from issuing from a pending patent application. As a result, the issuance, scope, validity and commercial value of our patent rights cannot be predicted with any certainty.

In addition, the patent prosecution process is expensive and time-consuming, and we or our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our licensors will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We cannot provide any assurances that we will be able to pursue or obtain additional patent protection based on our research and development efforts, or that any such patents or other intellectual property we generate will provide any competitive advantage. Patent prosecution is a lengthy process and the scope of the claims initially submitted for examination may be significantly narrowed by the time they issue, if at all. Moreover, we do not have the right to control the preparation, filing and prosecution of patent applications, or to control the maintenance of the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be filed, prosecuted or maintained in a manner consistent with the best interests of our business.

Even if we acquire patent protection that we expect should enable us to maintain competitive advantage, third parties, including competitors, may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability and our licensed patents may be challenged in courts or patent offices in the United States and abroad. For example, we may be subject to a third-party submission of prior art to the U.S. Patent and Trademark Office, or USPTO, challenging the validity of one or more claims of our licensed patents. Such submissions may also be made prior to a patent's issuance, precluding the granting of a patent based on one of our pending licensed patent applications. We may become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review, interference, or similar proceedings in the United States or abroad, challenging the patent rights of others from whom we have obtained licenses to such rights. Furthermore, our licensed patents may be challenged in district court. Competitors may claim that they invented the inventions claimed in such issued patents or patent applications prior to the inventors of our licensed patents, or may have filed patent applications before the inventors of our licensed patents did. A competitor may also claim that we are infringing its patents and that we therefore cannot practice our technology as claimed under our licensed patents, if issued. As a result, one or more claims of our licensed patents may be narrowed or invalidated.

Even if they are unchallenged, our licensed patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our licensed patents by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, even if we have a valid and enforceable patent, we may not be able to exclude others from practicing our invention if the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. Moreover, a third party may develop a competitive product that provides benefits similar to one or more of our product candidates but that uses a vector or an expression construct that falls outside the scope of our patent protection or license rights. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business. Although currently all of our patents and patent applications are in-licensed, similar risks would apply to any patents or patent applications that we may own or in-license in the future.

Our strategy of obtaining rights to key technologies through in-licenses may not be successful.

We seek to expand our product candidate pipeline in part by in-licensing the rights to key technologies, including those related to gene delivery. The future growth of our business will depend in part on our ability to in-license or otherwise acquire the rights to additional product candidates and technologies. There can be no assurance that we will be able to in-license or acquire the rights to any product candidates or technologies from third parties on acceptable terms or at all.

The in-licensing and acquisition of these technologies is a highly competitive area, and a number of more established companies are also pursuing strategies to license or acquire product candidates or technologies that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to license rights to us. Furthermore, we may be unable to identify suitable product candidates or technologies within our area of focus. If we are unable to successfully obtain rights to suitable product candidates or technologies, our business, financial condition and prospects could suffer.

If we breach our license agreements, it could have a material adverse effect on our commercialization efforts for our product candidates.

If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates or technology from third parties, we could lose license rights that are important to our business. We currently hold licenses or other rights for certain intellectual property, such as from REGENXBIO relating to various AAV vectors, from Genethon related to XLMTM, and from Nationwide Children's related to DMD and DM1.

Under our existing license agreements, we are subject to various obligations, including diligence obligations such as development and commercialization obligations, as well as potential royalty payments and other obligations. If we fail to comply with any of these obligations or otherwise breach our license agreements, our licensors may have the right to terminate the applicable license in whole or in part. Generally, the loss of any one of our current licenses, or any other license we may acquire in the future, could harm our business, prospects, financial condition and results of operations.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license 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 licensing agreement;
- our right to sublicense patent and other intellectual property rights to third parties under collaborative development relationships;
- 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; and
- whether and the extent to which inventors are able to contest the assignment of their rights to our licensors.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. In addition, if disputes arise as to ownership of licensed intellectual property, our ability to pursue or enforce the licensed patent rights may be jeopardized. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

All of our product candidates incorporate intellectual property licensed from or based upon licenses from third parties. If any of these license or sublicense agreements are terminated or interpreted to narrow our rights, or if we need to acquire of license additional patents or other intellectual property for our product candidates, our ability to advance our product candidates or develop new product candidates based on these technologies will be materially adversely affected.

We now depend, and will continue to depend, on licenses and sublicenses from third parties and potentially on other strategic relationships with third parties for the research, development, manufacturing and commercialization of our product candidates. If any of our licenses or relationships or any in-licenses on which our licenses are based are terminated or breached, we may:

- lose our rights to develop and market our product candidates;
- lose patent or trade secret protection for our product candidates;
- experience significant delays in the development or commercialization of our product candidates;
- not be able to obtain any other licenses on acceptable terms, if at all; or
- incur liability for damages.

Additionally, even if not terminated or breached, our intellectual property licenses or sublicenses may be subject to disagreements over contract interpretation which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations.

Moreover, licenses to additional third-party intellectual property, technology and materials may be required for our development programs but may not be available in the future or may not be available on commercially reasonable terms. For

example, our license agreements with REGENXBIO cover the use of certain AAV vectors for specific indications, including XLMTM and Pompe disease. We may need to enter into additional licenses to cover the use of the AAV vectors we use for our product candidates for the treatment of DMD and DM1 if the relevant patents are in force at the time of commercialization of our applicable product candidates. Such licenses may not be available on commercially reasonable terms, or at all. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to any third-party intellectual property rights that are required for the development and commercialization of any of our other product candidates, and such third-party intellectual property rights are successfully asserted against us, we may be liable for damages, which may be significant, and we may be required to cease the development and commercialization of such product candidates. Moreover, even if we are able to obtain such licenses, they may only be non-exclusive, which could permit competitors and other third parties to use the same intellectual property in competition with us.

If we experience any of the foregoing, it could have a materially adverse effect on our business and could force us to cease operations which could cause investors to lose all of their investment.

We are required to pay certain royalties under our license agreements with third-party licensors, and we must meet certain milestones to maintain our license rights.

Under our license agreements with REGENXBIO and our recently established license and collaboration agreement with Nationwide Children's, we will be required to pay royalties based on our net revenues from sales of our products utilizing the technologies. These royalty payments could adversely affect the overall profitability for us of any product candidates that we may seek to commercialize. In order to maintain our license rights under these license agreements, we will need to meet certain specified milestones, subject to certain cure provisions, in the development of our product candidates and in the raising of funding. In addition, these agreements contain development obligations and we may not be successful in meeting all of the obligations in the future on a timely basis or at all. We may need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our license agreements. Delay or failure by any such third parties could adversely affect the continuation of our license agreements with third-party licensors.

Third parties may initiate legal proceedings alleging claims of intellectual property infringement, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and future products and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and frequent litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates, future products and technology, including interference or *inter partes* review proceedings before the USPTO. Our competitors or other third parties may assert infringement or misappropriation claims against us, alleging that our therapeutics, manufacturing methods, formulations or administration methods are covered by their patents. For example, we do not know which processes we will use for commercial manufacture of our future products, or which technologies owned or controlled by third parties may prove important or essential to those processes. Given the vast number of patents in our field of technology, we cannot be certain or guarantee that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Many companies have filed, and continue to file, patent applications related to gene therapy and orphan diseases. Some of these patent applications have already been allowed or issued and others may issue in the future. Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use, sale or importation of our product candidates or future products. If a patent holder believes the manufacture, use, sale or importation of one of our product candidates or future products infringes its patent, the patent holder may sue us even if we have licensed other patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our licensed patent portfolio may therefore have no deterrent effect.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain

confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale, importation or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our future products or the manufacture or use of our future products.

Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future. For example, third parties may claim that the AAV vector we are developing for use in certain of our product candidates are covered by patents held by them. Even if we believe such claim, or other intellectual property claims alleged by third parties, are without merit, there is no assurance that we would be successful in defending such claims. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our ability to commercialize our product candidates covered by the asserted third-party patents. If we were to challenge the validity of an issued U.S. patent in court, such as an issued U.S. patent of potential relevance to some of our product candidates or future products or manufacture or methods of use, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found, or believe there is a risk we may be found, to infringe a third party's intellectual property rights, we could be required or may choose to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any such license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. Without such a license, we could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our future products or force us to cease some of our business operations, which could materially harm our business. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. If we lose a foreign patent lawsuit, alleging our infringement of a competitor's patents, we could be prevented from marketing our products in one or more foreign countries and/or be required to pay monetary damages for infringement or royalties in order to continue marketing. Claims that we have misappropriated the confidential information, trade secrets or other intellectual property of third parties could have a similar negative impact on our business. Any of these outcomes would have a materially adverse effect on our business.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our future products or processes. Patent litigation is costly and time-consuming, and some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. We may not have sufficient resources to bring these actions to a successful conclusion. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

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

In addition to the protection afforded by patents, we rely upon unpatented trade secret protection, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our contractors, collaborators, scientific advisors, employees and consultants and invention assignment agreements with our consultants and employees. We may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the contractors, collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. As a result, we could lose our trade secrets. Enforcing a claim that a third party illegally obtained and is

using our trade secrets, like patent litigation, is expensive and time consuming and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing or unwilling to protect trade secrets.

Our trade secrets could otherwise become known or be independently discovered by our competitors. Competitors could purchase our product candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. 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 our trade secrets are not adequately protected or sufficient to provide an advantage over our competitors, our competitive position could be adversely affected, as could our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional 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 a patent or patent application include, but are not limited to, failure to respond to official 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 product candidates, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our product candidates, which would have a material adverse effect on our business.

Some intellectual property that we have in-licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

Many of the intellectual property rights we have licensed are generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. In addition, the laws of some foreign countries do not protect intellectual property rights to the

same extent as federal and state laws in the United States. Further, licensing partners may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. For example, we have licensed certain intellectual property rights from Genethon, and the Genethon patent families were only filed in the United States, and therefore these patent families will not provide patent protection outside the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, 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. 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.

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

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we 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.

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 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 a material adverse effect on the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, enacted in September 2011, could increase those

uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a "first to file" system. The first-to-file provisions, however, only became effective in March 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

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. For example, in Association for Molecular Pathology v. Myriad Genetics, Inc., the Supreme Court ruled that a "naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated," and invalidated Myriad Genetics' patents on the BRCA1 and BRCA2 genes. Certain claims of our licensed patents relate to isolated AAV vectors, capsid proteins, or nucleic acids. To the extent that such claims are deemed to be directed to natural products, or to lack an inventive concept above and beyond an isolated natural product, a court may decide the claims are invalid under Myriad. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants or advisors, and the employees, consultants or advisors of our licensors, are currently, or were previously, employed at or affiliated with universities, hospitals or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Moreover, some of our and our licensors' employees, consultants or advisors are or have been affiliated with multiple institutions. There is no guarantee that such institutions will not challenge our or our licensors' intellectual property ownership rights. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or 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, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

We will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As our development, manufacturing and commercialization plans and strategies develop, and as we fully transition our operations to a mature public company, we expect to need and are actively recruiting additional managerial, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, and integrating new employees;
- retaining existing employees
- managing our internal development efforts effectively, including the clinical, FDA and international regulatory review process for our product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to develop, manufacture and commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert financial and other resources, and a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time, to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including substantially all aspects of clinical trials management. There can be no assurance that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the expertise of Matthew Patterson, our Chief Executive Officer, Natalie Holles, our President and Chief Operating Officer, and our other executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and manufacturing strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Recruiting and retaining qualified scientific, clinical, manufacturing and, if needed, sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles.

While our management has previously been, and will continue in the future to be, required to perform an evaluation of our internal control over financial reporting, our independent registered public accounting firm was not required to perform such an evaluation prior to the year ended December 31, 2018, which is the date we were no longer an emerging growth company. Accordingly, we are required to include in each of our Annual Reports on Form 10-K an attestation report on internal control over financial reporting issued by our independent registered accounting firm. There can be no assurance that we or our independent registered auditors will not in the future identify one or more material weaknesses in our internal control over financial reporting, which may have a negative impact on our ability to timely and accurately produce financial statements or which may negatively impact the confidence level of our stockholders and other market participants with respect to our ability to produce timely and accurate financial statements.

To the extent necessary, implementing any future changes to our internal controls may distract our executive officers and other employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to raise new capital or effectively market and sell our product candidates once they are approved for commercial sale.

We incur increased costs as a result of operating as a public company and our management is required to devote substantial time to compliance initiatives, each of which may increase now that we are no longer an emerging growth company.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company, which we expect will increase with the loss of our status as an "emerging growth company." In addition, the Sarbanes-Oxley Act of 2002 and rules implemented by the Securities and Exchange Commission and The Nasdaq Stock Market LLC, or Nasdaq, have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Furthermore, as of December 31, 2018, we became a "large accelerated filer" and are required to file our annual report and quarterly reports more quickly than we previously had been required to file them, which may require us to dedicate additional resources to the timely filing of such reports.

Additionally, as we are no longer an emerging growth company, we need to comply with additional disclosure and reporting requirements, including accelerated filing deadlines and an attestation report on internal control over financial reporting as of each fiscal year-end issued by our independent registered public accounting firm. We are also required to include additional information regarding executive compensation in our annual proxy statement and at our 2019 annual meeting of stockholders we will hold a nonbinding advisory vote on executive compensation at our annual meetings of stockholders. We will take into account the outcome of this vote in determining the frequency at which we conduct future nonbinding advisory votes on executive compensation.

Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time consuming and costly.

Future acquisitions or strategic alliances could disrupt our business and harm our financial condition and operating results.

We may acquire additional businesses or drugs, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. There can be no assurance that, following any such acquisition, we will achieve the expected synergies to justify the transaction. The risks we face in connection with acquisitions include:

- diversion of management time and focus from operating our business to addressing acquisition integration challenges;
- coordination of research and development efforts;
- retention of key employees from the acquired company;
- changes in relationships with strategic partners as a result of product acquisitions or strategic positioning resulting from the acquisition;
- cultural challenges associated with integrating employees from the acquired company into our organization;
- the need to implement or improve controls, procedures, and policies at a business that prior to the acquisition may have lacked sufficiently effective controls, procedures and policies;
- liability for activities of the acquired company before the acquisition, including intellectual property infringement claims, violation of laws, commercial disputes, tax liabilities, and other known liabilities;
- unanticipated write-offs or charges; and
- litigation or other claims in connection with the acquired company, including claims from terminated employees, customers, former stockholders or other third parties.

Our failure to address these risks or other problems encountered in connection with our past or future acquisitions or strategic alliances could cause us to fail to realize the anticipated benefits of these transactions, cause us to incur unanticipated

liabilities and harm the business generally. There is also a risk that future acquisitions will result in the incurrence of debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm our financial condition or operating results.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the 2008 global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the 2008 global financial crisis, or a prolonged government shutdown, could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services or products. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters, including earthquakes to which the San Francisco Bay Area is prone, could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, fire, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our manufacturing facilities, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time.

The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

Our internal computer and information systems, or those used by our CROs, third-party collaborators or other contractors, may fail or suffer security breaches, which could result in a material disruption of our development programs.

Despite the implementation of appropriate security measures, our internal computer and information systems and those of our current and any future CROs, collaborators and other contractors or consultants may become vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we do not believe we have experienced any such material system failure, or accident, and are unaware of any security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of data from completed or future preclinical studies or clinical trials could result in significant 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 confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be significantly delayed.

We may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential information, damage our reputation, and subject us to significant financial and legal exposure.

Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud and/or other means to threaten data confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, financial loss and the misappropriation of confidential business information, including financial information, trade secrets and corporate strategic plans. We do not believe we have experienced a material compromise of our data or information systems. However, although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our operating results and financial condition.

Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee 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 comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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

We will face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and will face an even greater risk if we commercialize any of our product candidates. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant time and costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any product candidates that we may develop.

We currently maintain product liability insurance coverage of up to $10.0 million, which may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we expand clinical trials and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or

import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Risks Related to Our Common Stock

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

Our stock price is likely to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell shares of our common stock at or above the price at which they purchased their shares. The market price for our common stock may be influenced by many factors, including:

- the success of competitive drugs or technologies;
- results of preclinical studies or clinical trials of our product candidates or those of our competitors;
- unanticipated or serious safety concerns related to the use of any of our product candidates;
- adverse regulatory decisions, including failure to receive regulatory approval for any of our product candidates;
- regulatory or legal developments in the United States and other countries;
- the size and growth of our prospective patient populations;
- developments concerning our collaborators, our external manufacturers or in-house manufacturing capabilities;
- inability to obtain adequate product supply for any product candidate for preclinical studies, clinical trials or future commercial sale or inability to do so at acceptable prices;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the biotechnology sector;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock depends in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable evaluations of our company or our stock, the price of our stock could decline. If one or more of these analysts ceases to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital may be needed in the future to continue our planned operations, including conducting our planned clinical trials, manufacturing and commercialization efforts, expanded research and development activities and costs associated with operating as a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. These

sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

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

We have never declared or paid any cash dividends on our common stock and do not currently intend to do so for the foreseeable future. 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. Any return to stockholders will be limited to the appreciation of stock. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in value of the stock. There can be no assurance that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased their shares.

Our amended and restated certificate of incorporation designates the Court of Chancery of the State of Delaware as the sole and exclusive forum 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 amended and restated certificate of incorporation provides that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, or DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws or any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein and the claim not being one which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery or for which the Court of Chancery does not have subject matter jurisdiction. Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our amended and restated certificate of incorporation. This choice of forum provision may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers, employees or agents, which may discourage such lawsuits against us and our directors, officers, employees and agents even though an action, if successful, might benefit our stockholders. Stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near Delaware. The Court of Chancery may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. Alternatively, if a court were to find this provision of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have a material adverse effect on our business, financial condition or results of operations.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our amended and restated certificate of incorporation and amended and restated bylaws;

- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan, also known as a "poison pill";
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

Moreover, we are governed by the provisions of Section 203 of the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any of these provisions of our charter documents or Delaware law could, under certain circumstances, depress the market price of our common stock.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed/Furnished Herewith
		Form	File No.	Exhibit Filing Date	
31.1	Certification of Principal Executive Officer, pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of Principal Financial Officer, pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1*	Certification of Chief Executive Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
32.2*	Certification of Chief Financial Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
101.INS	XBRL Instance Document.				X
101.SCH	XBRL Taxonomy Extension Schema Document.				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.				X
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document.				X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.				X

* This certification is deemed not filed for purpose of section 18 of the Exchange Act or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.

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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.

AUDENTES THERAPEUTICS, INC.

Date: May 7, 2019

By: /s/ Matthew Patterson

Matthew Patterson
Chairman and Chief Executive Officer
(Principal Executive Officer)

Date: May 7, 2019

By: /s/ Thomas Soloway

Thomas Soloway
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 31.1

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Matthew Patterson, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Audentes Therapeutics, 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: May 7, 2019

/s/ Matthew Patterson

Matthew Patterson
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Tom Soloway, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Audentes Therapeutics, 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: May 7, 2019

/s/ Tom Soloway

Tom Soloway
Chief Financial Officer
(Principal Executive Officer)

Exhibit 32.1

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

I, Matthew Patterson, Chief Executive Officer of Audentes Therapeutics, Inc. (Company), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

- the Quarterly Report on Form 10-Q of the Company for the quarter ended March 31, 2019 (Report), as filed with the Securities and Exchange Commission, fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the periods presented therein.

Date: May 7, 2019

/s/ Matthew Patterson

Matthew Patterson
Chief Executive Officer
(Principal Executive Officer*)*

Exhibit 32.2

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

I, Tom Soloway, Chief Financial Officer of Audentes Therapeutics, Inc. (Company), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

- the Quarterly Report on Form 10-Q of the Company for the quarter ended March 31, 2019 (Report), as filed with the Securities and Exchange Commission, fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the periods presented therein.

Date: May 7, 2019

/s/ Tom Soloway

Tom Soloway
Chief Financial Officer
(Principal Financial Officer)