
**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 June 30, 2018.

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: 001-37625

Voyager Therapeutics, Inc.
(Exact name of Registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

**75 Sidney Street,
Cambridge, Massachusetts**
(Address of principal executive offices)

46-3003182
(I.R.S. Employer
Identification No.)

02139
(Zip Code)

(857) 259-5340
(Registrant's telephone number, including area code)

Not Applicable
(Former name, former address and former fiscal year, if changed since last report)

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post 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	<input type="checkbox"/>	(Do not check if a smaller reporting company)	Accelerated filer	<input checked="" type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>		Smaller reporting company	<input type="checkbox"/>
	<input type="checkbox"/>		Emerging growth company	<input checked="" type="checkbox"/>

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

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

The number of outstanding shares of the registrant's common stock, par value \$0.001 per share, as of August 3, 2018 was 32,436,009.

Forward Looking Statements

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “predict,” “project,” “target,” “potential,” “contemplate,” “anticipate,” “goals,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- our plans to develop and commercialize our product candidates based on adeno-associated virus, or AAV, gene therapy;
- our ability to identify and optimize product candidates and novel AAV gene therapy capsids;
- our ongoing and planned clinical trials and related timelines, including our ability to continue to advance VY-AADC through the ongoing Phase 1b clinical trial and into the pivotal Phase 2-3 clinical program as a treatment for Parkinson’s disease, and our preclinical development efforts and studies;
- formulation changes to our product candidates may require us to conduct additional clinical studies to bridge our modified product candidates to earlier versions;
- the timing of and our ability to submit applications for, and obtain and maintain regulatory approvals for our product candidates, including our ability to file Investigational New Drug applications for our programs including VY-SOD101 for the treatment of a monogenic form of amyotrophic lateral sclerosis, VY-HTT01 for the treatment of Huntington’s disease, and VY-FXN01 for the treatment of Friedreich’s ataxia;
- our estimates regarding expenses, future revenues, capital requirements, and needs for additional financing;
- our ability to continue to develop our gene therapy platform;
- our ability to develop a manufacturing capability compliant with current good manufacturing practices for our product candidates;
- our ability to access, develop, and obtain regulatory clearance for devices to deliver our AAV gene therapies to critical targets of neurological disease;
- our intellectual property position and our ability to obtain and maintain intellectual property protection for our proprietary assets;
- our estimates regarding the size of the potential markets for our product candidates and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates for any indication once approved;
- our strategic collaborations with Sanofi Genzyme and AbbVie Biotechnology Ltd, including the possibility and timing of each exercising options to certain of our programs as specified in the applicable collaboration agreements;
- our plans and ability to raise additional capital, including through equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements;

- our competitive position and the success of competing products that are or become available for the indications that we are pursuing;
- the impact of government laws and regulations including in the United States, the European Union, and other important geographies such as Japan;
- our ability to maintain consistency with results from our ongoing Phase 1b clinical trial and our separate Phase 1 trial focused on posterior trajectory in future clinical trials; and
- our ability to enter into future collaborations, strategic alliances, or licensing arrangements.

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements. You should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. 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 business, financial condition and operating results. We have included important factors in the cautionary statements included in this Quarterly Report on Form 10-Q, particularly in “Part II, Item 1A - Risk Factors,” and in “Part I, Item 1A – Risk Factors” included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 14, 2018, that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Quarterly Report on Form 10-Q and the documents that we have filed as exhibits to this Quarterly Report on Form 10-Q with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

VOYAGER THERAPEUTICS, INC.

FORM 10-Q

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PART I. FINANCIAL INFORMATION

Voyager Therapeutics, Inc.
Condensed Consolidated Balance Sheets
(amounts in thousands, except share and per share data)
(unaudited)

	<u>June 30,</u> <u>2018</u>	<u>December 31,</u> <u>2017</u>
Assets		
Current assets:		
Cash and cash equivalents	\$ 59,614	\$ 31,530
Marketable securities, current	136,509	137,522
Prepaid expenses and other current assets	4,122	2,738
Total current assets	<u>200,245</u>	<u>171,790</u>
Property and equipment, net	12,244	10,283
Deposits and other non-current assets	1,314	1,304
Marketable securities, non-current	860	1,100
Total assets	<u>\$ 214,663</u>	<u>\$ 184,477</u>
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 1,558	\$ 1,020
Accrued expenses	7,697	11,497
Deferred revenue, current portion	19,840	3,380
Total current liabilities	29,095	15,897
Deferred rent	5,282	5,337
Deferred revenue, net of current portion	97,308	28,180
Other non-current liabilities	1,006	1,012
Total liabilities	<u>132,691</u>	<u>50,426</u>
Commitments and contingencies (see note 6)		
Stockholders' equity:		
Preferred stock \$0.001 par value: 5,000,000 shares authorized at June 30, 2018 and December 31, 2017; no shares issued and outstanding at June 30, 2018 and December 31, 2017	—	—
Common stock, \$0.001 par value: 120,000,000 shares authorized at June 30, 2018 and December 31, 2017; 32,063,948 and 31,572,044 shares issued and outstanding at June 30, 2018 and December 31, 2017, respectively	32	32
Additional paid-in capital	308,296	295,019
Accumulated other comprehensive loss	(125)	(287)
Accumulated deficit	<u>(226,231)</u>	<u>(160,713)</u>
Total stockholders' equity	81,972	134,051
Total liabilities and stockholders' equity	<u>\$ 214,663</u>	<u>\$ 184,477</u>

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

Voyager Therapeutics, Inc.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(amounts in thousands, except share and per share data)
(unaudited)

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2018	2017	2018	2017
Collaboration revenue	\$ 2,575	\$ 1,177	\$ 3,517	\$ 2,642
Operating expenses:				
Research and development	16,507	15,300	31,360	29,372
General and administrative	11,762	4,516	18,945	9,430
Total operating expenses	<u>28,269</u>	<u>19,816</u>	<u>50,305</u>	<u>38,802</u>
Operating loss	(25,694)	(18,639)	(46,788)	(36,160)
Other income (expense):				
Interest income, net	870	255	1,458	508
Other (expense) income, net	(717)	(297)	(318)	98
Total other income (expense)	<u>153</u>	<u>(42)</u>	<u>1,140</u>	<u>606</u>
Loss before income taxes	(25,541)	(18,681)	(45,648)	(35,554)
Income tax (provision) benefit	—	(195)	180	31
Net loss	<u>\$ (25,541)</u>	<u>\$ (18,876)</u>	<u>\$ (45,468)</u>	<u>\$ (35,523)</u>
Other comprehensive income (loss)				
Unrealized gain (loss) on available-for-sale- securities, net of income tax (benefit) provision of \$(191) and \$53 for the three and six months ended June 30, 2017, respectively	37	(295)	157	82
Total other comprehensive income (loss)	<u>37</u>	<u>(295)</u>	<u>157</u>	<u>82</u>
Comprehensive loss	<u>\$ (25,504)</u>	<u>\$ (19,171)</u>	<u>\$ (45,311)</u>	<u>\$ (35,441)</u>
Net loss per share, basic and diluted	<u>\$ (0.80)</u>	<u>\$ (0.73)</u>	<u>\$ (1.43)</u>	<u>\$ (1.37)</u>
Weighted-average common shares outstanding, basic and diluted	<u>31,976,922</u>	<u>25,946,333</u>	<u>31,868,995</u>	<u>25,869,390</u>

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

Voyager Therapeutics, Inc.
Condensed Consolidated Statements of Cash Flows
(amounts in thousands)
(unaudited)

	Six Months Ended	
	June 30,	
	2018	2017
Cash flow from operating activities		
Net loss	\$ (45,468)	\$ (35,523)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Stock-based compensation expense	10,436	3,704
Depreciation	972	726
Amortization of premiums and discounts on marketable securities	(908)	169
In-kind research and development expenses	176	113
Other non-cash items	355	(144)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,384)	965
Other non-current assets	(180)	—
Deferred revenue	65,482	(2,642)
Accounts payable	538	(243)
Accrued expenses	(3,911)	731
Other non-current liabilities	—	1,000
Lease incentive benefit	—	515
Net cash provided by (used in) operating activities	<u>26,108</u>	<u>(30,629)</u>
Cash flow from investing activities		
Purchases of property and equipment	(2,933)	(3,412)
Purchases of marketable securities	(205,037)	—
Proceeds from maturities of marketable securities	207,000	62,600
Net cash (used in) provided by investing activities	<u>(970)</u>	<u>59,188</u>
Cash flow from financing activities		
Proceeds from the exercise of stock options	2,528	1,100
Proceeds from the purchase of common stock under ESPP	418	—
Net cash provided by financing activities	<u>2,946</u>	<u>1,100</u>
Net increase in cash, cash equivalents, and restricted cash	28,084	29,659
Cash, cash equivalents, and restricted cash beginning of period	32,265	37,376
Cash, cash equivalents, and restricted cash end of period	<u>\$ 60,349</u>	<u>\$ 67,035</u>
Supplemental disclosure of cash and non-cash activities		
Capital expenditures incurred but not yet paid	\$ —	\$ 95
Impact of adopting new accounting standards	\$ 20,050	\$ —

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

VOYAGER THERAPEUTICS, INC.

NOTES TO UNAUDITED CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of business

Voyager Therapeutics, Inc. (the “Company”) is a clinical-stage gene therapy company focused on developing life-changing treatments for patients suffering from severe neurological diseases. The Company is focused on neurological diseases where it believes an adeno-associated virus (“AAV”) gene therapy approach that either increases or decreases the production of a specific protein can slow or reduce the symptoms experienced by patients, and therefore have a clinically meaningful impact. The Company has built a gene therapy platform that it believes positions itself to be a leading company at the intersection of AAV gene therapy and severe neurological disease. The Company’s gene therapy platform enables it to engineer, optimize, manufacture and deliver its AAV-based gene therapies that have the potential to provide durable efficacy following a single administration.

Additionally, the Company is working to identify novel AAV capsids, which are the outer viral protein shells that enclose the genetic material of the virus payload. The Company’s team of experts in the fields of AAV gene therapy and neuroscience first identifies and selects severe neurological diseases that are well-suited for treatment using AAV gene therapy. The Company then engineers and optimizes AAV vectors for delivery of the virus payload to the targeted tissue or cells. The Company’s manufacturing process employs an established system that it believes will enable production of high quality AAV vectors at commercial-scale. Finally, the Company leverages established routes of administration and advances in dosing techniques to optimize delivery of its AAV gene therapies to target cells that are critical to the disease of interest, either directly to discrete regions of the brain, or, more broadly, to the spinal cord region.

The Company’s business strategy focuses on discovering, developing, manufacturing and commercializing its gene therapy programs. As part of this strategy, the Company has developed core competencies specific to AAV gene therapy development and manufacturing and is beginning to build its commercial infrastructure. This business strategy also includes business development activities that may include in-licensing activities or partnering certain programs in certain geographies with collaborators, as the Company has demonstrated through its collaboration with Sanofi Genzyme (the “Sanofi Genzyme Collaboration”) and its collaboration with AbbVie Biotechnology Ltd (the “AbbVie Collaboration”). The Company is devoting substantially all of its efforts to product research and development, market development, and raising capital. The Company is subject to risks common to companies in the biotechnology and gene therapy industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for its product candidates, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations, and ability to transition from pilot-scale manufacturing to large-scale production of products.

The Company has incurred annual net operating losses in every year since inception. As of June 30, 2018, the Company had an accumulated deficit of \$226.2 million. The Company has not generated any product revenue and has financed its operations primarily through public offerings and private placements of its equity securities and funding from the Sanofi Genzyme Collaboration and the AbbVie Collaboration. There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate product revenue or revenue from collaborative partners on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company’s business, results of operations, and financial condition.

Through June 30, 2018, the Company has raised approximately \$405.0 million of proceeds from sales of convertible preferred stock and common stock, including its initial public offering (the “IPO”) and follow-on public offering, and from collaboration agreements. The Company believes that its cash, cash equivalents, and marketable debt securities of \$197.0 million as of June 30, 2018 is sufficient to fund its current operating plan into early 2020. There can be no assurance, however, that the current operating plan will be achieved in the timeframe anticipated by the Company,

or that its cash resources will fund the Company's operating plan for the period anticipated by the Company, or if the Company needs additional funding, that such funding will be available on terms acceptable to the Company, or at all.

2. Summary of significant accounting policies and basis of presentation

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements of the Company have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP") for interim financial reporting and as required by Regulation S-X, Rule 10-01. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. For further information, refer to the consolidated financial statements and footnotes included in the Company's Annual Report on Form 10-K for the year ended December 31, 2017 as filed with the Securities and Exchange Commission ("SEC"). These interim condensed consolidated financial statements, in the opinion of management, reflect all normal recurring adjustments necessary for a fair presentation of the Company's financial position and results of operations for the periods presented. Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Principles of Consolidation

The unaudited interim consolidated financial statements include the accounts of the Company and its wholly owned subsidiary as disclosed in Note 2, Summary of Significant Accounting Policies, within the "Notes to Consolidated Financial Statements" accompanying its Annual Report on Form 10-K for the fiscal year ended December 31, 2017. Intercompany accounts and transactions have been eliminated.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to revenue recognition, accrued expenses, stock-based compensation expense, income taxes, and the fair value of common stock. The Company bases its estimates on historical experience and other market specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Revenue Recognition

The Company enters into collaboration agreements which are within the scope of ASC 606, *Revenue from Contracts with Customers* ("ASC 606"), under which the Company licenses rights to certain of the Company's product candidates and performs research and development services. The terms of these arrangements typically include payment of one or more of the following: non-refundable, upfront fees; reimbursement of research and development costs; development, regulatory, and commercial milestone payments; and royalties on net sales of licensed products.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, the Company performs the following five steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect consideration it is entitled to in exchange for the goods or services it transfers to the customer.

The promised goods or services in the Company's arrangement typically consist of license rights to the Company's intellectual property and research and development services. The Company provides options to additional items in the contracts, which are accounted for as separate contracts when the customer elects to exercise such options, unless the option provides a material right to the customer. The Company evaluates the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer and are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on its own or whether the required expertise is readily available and whether the goods or services are integral or dependent to other goods or services in the contract.

The Company estimates the transaction price based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration may include fixed consideration or variable consideration. At the inception of each arrangement that includes variable consideration, the Company evaluates the amount of potential payments and the likelihood that the payments will be received. The Company utilizes either the most likely amount method or expected amount method to estimate the amount expected to be received based on which method best predicts the amount expected to be received. The amount of variable consideration which is included in the transaction price may be constrained, and is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period.

The Company's contracts often include development and regulatory milestone payments which are assessed under the most likely amount method and constrained if it is probable that a significant revenue reversal would occur. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues in the period of adjustment. To date, the Company has not recognized any consideration related to the achievement of development, regulatory, or commercial milestone revenue resulting from any of the Company's collaboration arrangements.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any consideration related to sales-based royalty revenue resulting from any of the Company's collaboration arrangements.

The Company allocates the transaction price based on the estimated stand-alone selling price of each of the performance obligations. The Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company utilizes key assumptions to determine the stand-alone selling price for service obligations, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. Additionally, in determining the standalone selling price for material rights, the Company utilizes comparable transactions, clinical trial success probabilities, and estimates of option exercise likelihood. Variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated are consistent with the amounts the Company would expect to receive for the satisfaction of each performance obligation.

The consideration allocated to each performance obligation is recognized as revenue when control is transferred for the related goods or services. For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of

measuring progress. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Upfront payments and fees are recorded as deferred revenue upon receipt or when due until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional.

Recently Adopted Accounting Pronouncements

In January 2016, the FASB issued ASC Update No. 2016-01, *Financial Instruments - Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities* ("Update No. 2016-01"). The purpose of Update No. 2016-01 is to improve financial reporting for financial instruments by reducing the number of items recorded to other comprehensive income. The Company adopted Update No. 2016-01 in the first quarter of 2018, using the modified retrospective method. Unrealized gains and losses previously recorded to other comprehensive income (loss) were reclassified to accumulated deficit and all future fair value changes will be recorded to other income (loss). The adoption of the standard on January 2, 2018 did not have a material impact on the Company's consolidated financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows* ("ASU 2016-15"), which simplifies certain elements of cash flow classification and is intended to reduce diversity in practice in how certain transactions are classified in the statement of cash flows. The update is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017. The Company adopted ASU 2016-15 on January 1, 2018, and such adoption did not have a material impact on the Company's consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash* ("ASU 2016-18"). The amendments in ASU 2016-18 require an entity to reconcile and explain the period-over-period change in total cash, cash equivalents and restricted cash within its statements of cash flows and was applied utilizing a full retrospective approach. The Company adopted the new standard on January 1, 2018. The Company has included the necessary reconciliation within Note 4 "Cash, cash equivalents, and available-for-sale marketable securities."

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* ("ASU 2014-09"), which supersedes the revenue recognition requirements in ASC 605, *Revenue Recognition* ("ASC 605"), and most industry-specific guidance. The new standard requires that an entity recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The update also requires additional disclosure about the nature, amount, timing, and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. Thereafter, a series of clarifying ASUs, narrow scope improvements and practical expedients were issued. This collective guidance resulted in the new revenue standard, ASC 606. ASC 606 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017 and should be applied retroactively to each prior reporting period presented or retrospectively with the cumulative effect of initially applying this update recognized at the date of initial application.

The Company adopted the new standard effective January 1, 2018 using the modified retrospective approach. The Company had one open contract, relating to the Sanofi Genzyme Collaboration, on the adoption date and has assessed it under the new revenue standard. The adoption of ASC 606 resulted in the changes to (i) the allocation of arrangement consideration, including the determination of estimated selling price and the allocation of variable consideration to specific performance obligations and (ii) the application of proportional performance as a measure of progress on service related deliverables.

The Company has accounted for the impact of adopting ASC 606 as a cumulative catch-up under the modified retrospective approach, which is represented as an increase of \$20.0 million to deferred revenue with an offset to accumulated deficit, effective January 1, 2018. The following financial statement line items have been shown to reflect comparative balances under ASC 606 and ASC 605 for each of the three-month period and six-month period ended June 30, 2018, for both of the Sanofi Genzyme Collaboration and AbbVie Collaboration, collectively.

Condensed Consolidated Statements of Operations and Comprehensive Loss

	Three months ended June 30, 2018		
	Under ASC 606	Under ASC 605	Effect of change
	(in thousands, except per share data)		
Collaboration revenue	\$ 2,575	\$ 2,908	\$ (333)
Loss before income taxes	(25,541)	(25,208)	(333)
Net loss	(25,541)	(25,208)	(333)
Net loss per share, basic and diluted	(0.80)	(0.79)	(0.01)

	Six months ended June 30, 2018		
	Under ASC 606	Under ASC 605	Effect of change
	(in thousands, except per share data)		
Collaboration revenue	\$ 3,517	\$ 4,213	\$ (696)
Loss before income taxes	(45,648)	(44,952)	(696)
Net loss	(45,468)	(44,772)	(696)
Net loss per share, basic and diluted	(1.43)	(1.40)	(0.03)

Condensed Consolidated Balance Sheets

	As of June 30, 2018		
	Under ASC 606	Under ASC 605	Effect of change
	(in thousands)		
Deferred revenue, current	\$ 19,840	\$ 17,819	\$ 2,021
Deferred revenue, non-current	97,308	78,703	18,605
Accumulated deficit	(226,231)	(205,605)	(20,626)

Condensed Consolidated Statements of Cash Flows

	Six months ended June 30, 2018		
	Under ASC 606	Under ASC 605	Effect of change
	(in thousands)		
Net loss	\$ (45,468)	\$ (44,772)	\$ (696)
Adjustments to reconcile net loss to net cash provided by operating activities:			
Deferred revenue	65,482	64,786	696

Recent Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, a comprehensive new lease accounting standard, which provides revised guidance on accounting for lease arrangements by both lessors and lessees and requires lessees to recognize a lease liability and a right-of-use asset for most leases. The new guidance is effective for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years, with early adoption permitted. The new standard must be applied using a modified retrospective transition approach which requires application of the new

guidance for all periods presented. The Company is currently in the process of evaluating the impact that the adoption of this guidance will have on its consolidated financial statements and related disclosures.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 (“SAB 118”), to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Cuts and Jobs Act, or the Tax Reform Act. The Company has recognized the provisional tax impacts related to the revaluation of the deferred tax assets and liabilities and included these amounts in its consolidated financial statements for the year ended December 31, 2017. The ultimate impact may differ from these provisional amounts due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued, and actions the Company may take as a result of the Tax Reform Act. The accounting is expected to be complete when the Company’s 2017 U.S. corporate income tax return is filed in 2018.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation-Stock Compensation (“ASC 718”): Improvements to Nonemployee Share-Based Payment Accounting*. The new standard largely aligns the accounting for share-based payment awards issued to employees and nonemployees by expanding the scope of ASC 718 to apply to nonemployee share-based transactions, as long as the transaction is not effectively a form of financing. The new guidance will be effective for the Company on January 1, 2019. The Company is currently evaluating the potential impact that this guidance may have on its consolidated financial statements.

3. Fair value measurements

Assets and liabilities measured at fair value on a recurring basis as of June 30, 2018 and December 31, 2017 are as follows:

Assets	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
(in thousands)				
June 30, 2018				
Money market funds included in cash and cash equivalents	\$ 58,458	\$ 58,458	\$ —	\$ —
Marketable securities:				
U.S. Treasury notes	136,509	136,509	—	—
Equity securities	860	860	—	—
Total marketable securities	<u>\$ 137,369</u>	<u>\$ 137,369</u>	<u>\$ —</u>	<u>\$ —</u>
Warrants to purchase equity securities	400	—	400	—
Total	<u>\$ 196,227</u>	<u>\$ 195,827</u>	<u>\$ 400</u>	<u>\$ —</u>
December 31, 2017				
Money market funds included in cash and cash equivalents	\$ 30,469	\$ 30,469	\$ —	\$ —
Marketable securities:				
U.S. Treasury notes	137,522	137,522	—	—
Equity securities	1,100	1,100	—	—
Total marketable securities	<u>\$ 138,622</u>	<u>\$ 138,622</u>	<u>\$ —</u>	<u>\$ —</u>
Warrants to purchase equity securities	569	—	569	—
Total	<u>\$ 169,660</u>	<u>\$ 169,091</u>	<u>\$ 569</u>	<u>\$ —</u>

The Company measures the fair value of money market funds, U.S. Treasury notes and equity securities based on quoted prices in active markets for identical securities. The Level 2 equity securities include warrants used to purchase equity securities that are valued using the Black-Scholes model. The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the awards, (c) the risk-free interest rate, and (d) expected dividends. The assumptions

utilized to value the warrants to purchase equity securities of the Company as of June 30, 2018 and December 31, 2017 are as follows:

	<u>As of June 30,</u> <u>2018</u>	<u>As of December 31,</u> <u>2017</u>
Risk-free interest rate	2.6 %	2.0 %
Expected dividend yield	— %	— %
Expected term (in years)	3.2	3.7
Expected volatility	108.9 %	103.5 %

The expected volatility is based on the historic volatility for the equity securities of the Company underlying the warrants and is calculated based on a period of time commensurate with the expected term assumption. The expected term is based on the remaining contractual life of the warrants on each measurement date. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the warrants. The expected dividend yield is assumed to be zero as the entity that issued the warrants has never paid and has not indicated any intention to pay dividends.

4. Cash, cash equivalents, and available-for-sale marketable securities

Cash equivalents include all highly liquid investments maturing within 90 days from the date of purchase. Investments consist of securities with original maturities greater than 90 days when purchased. The Company classifies these investments as available-for-sale and records them at fair value in the accompanying condensed consolidated balance sheets. Unrealized gains or losses are included in accumulated other comprehensive income (loss). Premiums or discounts from par value are amortized to investment income over the life of the underlying investment.

The Company classifies marketable debt securities with a remaining maturity when purchased of greater than three months as available-for-sale. Marketable debt securities with a remaining maturity date greater than one year and marketable equity securities are classified as non-current where the Company has the intent and ability to hold these securities for at least the next 12 months. Available-for-sale debt securities are maintained by an investment manager and consist of U.S. Treasury notes. In 2016, the Company invested in a supplier and received common stock and warrants to purchase common stock in that entity. The common stock is included in non-current marketable securities and the warrants are included in non-current assets.

Realized gains and losses are determined using the specific identification method and are included in other income (expense). If any adjustment to fair value reflects a decline in value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is “other-than-temporary” and, if so, recognizes the unrealized loss through a charge to the Company’s statement of operations and comprehensive loss. No other-than-temporary losses have been recognized.

Cash, cash equivalents, and marketable securities included the following at June 30, 2018 and December 31, 2017:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(in thousands)			
As of June 30, 2018				
Money market funds included in cash and cash equivalents	\$ 58,458	\$ —	\$ —	\$ 58,458
Marketable securities:				
U.S. Treasury notes	136,506	5	2	136,509
Equity securities	1,220	—	360	860
Total marketable securities	\$ 137,726	\$ 5	\$ 362	\$ 137,369
Total money market funds and marketable securities	\$ 196,184	\$ 5	\$ 362	\$ 195,827
As of December 31, 2017				
Money market funds included in cash and cash equivalents	\$ 30,469	\$ —	\$ —	\$ 30,469
Marketable securities:				
U.S. Treasury notes	137,560	—	38	137,522
Equity securities	1,220	—	120	1,100
Total marketable securities	\$ 138,780	\$ —	\$ 158	\$ 138,622
Total money market funds and marketable securities	\$ 169,249	\$ —	\$ 158	\$ 169,091

All of the Company's marketable debt securities at June 30, 2018, have a contractual maturity of one year or less.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash within the statement of financial position that sum to the total of the same such amounts shown in the statement of cash flows:

	As of June 30, 2018	As of December 31, 2017
	(in thousands)	
Cash and cash equivalents	\$ 59,614	\$ 31,530
Restricted cash included in deposits and other noncurrent assets	735	735
Total cash, cash equivalents, and restricted cash	\$ 60,349	\$ 32,265

5. Accrued expenses

Accrued expenses as of June 30, 2018 and December 31, 2017 consist of the following:

	As of June 30, 2018	As of December 31, 2017
	(in thousands)	
Research and development costs	\$ 3,928	\$ 5,780
Employee compensation costs	2,354	3,383
Professional services	896	1,762
Accrued goods and services	363	388
Patent costs	100	120
Other	56	64
Total	\$ 7,697	\$ 11,497

6. Commitments and contingencies

Operating Leases

In April 2014, the Company entered into an agreement to lease a facility at 75 Sidney Street under a non-cancelable operating lease that would expire December 15, 2019. The lease includes two renewal options, each for five-year terms and at fair market value upon exercise. The lease contains escalating rent clauses which require higher rent payments in future years. The Company expenses rent on a straight-line basis over the term of the lease, including any rent-free periods.

In December 2015, the Company executed an amendment to the 75 Sidney Street lease to extend its term, and executed an agreement to lease a facility at 64 Sidney Street until December 31, 2024. The facility at 64 Sidney Street includes laboratory and office space, and was ready for occupancy in early 2017.

In February 2018, the Company executed a second amendment to the 75 Sidney Street lease to lease additional space to support its continued growth. The additional facility includes laboratory and office space, and was ready for occupancy in mid-2018.

In June 2018, the Company executed a third amendment to the 75 Sidney Street lease to lease additional space to further support its continued growth. The additional facility will include laboratory and office space, and will be ready for occupancy in late 2018. The third amendment extended the term of the 75 Sidney Street lease until November 30, 2026. Additionally, the Company executed a second amendment to the 64 Sidney Street lease to extend that lease until November 30, 2026.

The Company received leasehold improvement incentives from the landlord of both leased properties totaling \$1.3 million and \$3.5 million for 75 Sidney Street and 64 Sidney Street, respectively, as of June 30, 2018. The Company recorded these incentives as a component of deferred rent and is amortizing these incentives as a reduction of rent expense over the life of the leases. The leasehold improvements have been recorded as fixed assets. The Company is entitled to receive approximately \$0.6 million of leasehold improvements for the additional space at 75 Sidney Street.

The following table summarizes the Company's significant contractual obligations as of payment due date by period at June 30, 2018, related to the amended 75 Sidney Street lease and the amended 64 Sidney Street lease through December 2026:

	Total Minimum Lease Payments
	(in thousands)
2018 (remainder of year)	\$ 2,110
2019	4,325
2020	4,731
2021	4,863
2022	5,001
2023+	21,924
	<u>\$ 42,954</u>

Significant Agreements

Sanofi Genzyme Collaboration Agreement

Summary of Agreement

In February 2015, the Company entered into a collaboration agreement with Sanofi Genzyme (the "Sanofi Genzyme Collaboration Agreement"), which included a non-refundable upfront payment of \$65.0 million. In addition, contemporaneously with entering into the Sanofi Genzyme Collaboration Agreement, Sanofi Genzyme entered into a Series B Stock Purchase Agreement, under which Sanofi Genzyme purchased 10,000,000 shares of Series B Preferred

Stock for \$30.0 million. The fair value of the Series B Preferred Stock at the time of issuance was approximately \$25.0 million. The \$5.0 million premium over the fair value is accounted for as additional consideration under the Sanofi Genzyme Collaboration Agreement.

Under the Sanofi Genzyme Collaboration Agreement, the Company granted Sanofi Genzyme an exclusive option to license, develop and commercialize (i) ex-U.S. rights to the following programs, which are referred to as “Split Territory Programs”; VY-AADC (“Parkinson’s Program”), VY-FXN01 (“Friedreich’s Ataxia Program”), a future program to be designated by Sanofi Genzyme (“Future Program”), and VY-HTT01 (“Huntington’s Program”) with an incremental option to co-commercialize VY-HTT01 in the United States and (ii) worldwide rights to VY-SMN101 (“Spinal Muscular Atrophy Program”). Sanofi Genzyme’s option for the Split Territory Programs and the Spinal Muscular Atrophy Program is triggered following the completion of the first proof of principle human clinical study (“POP Study”), on a program-by-program basis.

Prior to any option exercise by Sanofi Genzyme, the Company will collaborate with Sanofi Genzyme in the development of products under each Split Territory Program and/or the Spinal Muscular Atrophy Program pursuant to a written development plan and under the guidance of an Alliance Joint Steering Committee (“AJSC”), comprised of an equal number of employees from the Company and Sanofi Genzyme.

The Company is required to use commercially reasonable efforts to develop products under each Split Territory Program and the Spinal Muscular Atrophy Program through the completion of the applicable POP Study. During the development of these joint programs, the activities are guided by a Development Advisory Committee (“DAC”). The DAC may elect to utilize certain Sanofi Genzyme technology relating to the Parkinson’s Program, the Huntington’s Program, or generally with the manufacture of Split Territory Program products.

The Company is solely responsible for all costs incurred in connection with the development of the Split Territory Programs and the Spinal Muscular Atrophy Program products prior to the exercise of an option by Sanofi Genzyme with the exception of the following: (i) at the Company’s request and upon mutual agreement, Sanofi Genzyme will provide “in-kind” services valued at up to \$5.0 million and (ii) Sanofi Genzyme shall be responsible for the costs and expenses of activities under the Huntington’s Program development plan to the extent such activities are covered by financial support Sanofi Genzyme is entitled to receive from a patient advocacy group.

Other than the Parkinson’s Program (for which a POP Study has already been completed), if the Company does not initiate a POP Study for a given Split Territory Program by December 31, 2026 (or for the Future Program by the tenth anniversary of the date the Future Program is nominated by Sanofi Genzyme), and Sanofi Genzyme has not terminated the Sanofi Genzyme Collaboration Agreement with respect to the collaboration program, then Sanofi Genzyme shall be entitled, as its sole and exclusive remedy, to a credit of \$10.0 million for each such program against other milestone or royalty payments payable by Sanofi Genzyme under the Sanofi Genzyme Collaboration Agreement. However, if the POP Study is not initiated due to a regulatory delay or a force majeure event, such time period shall be extended for so long as such delay continues.

With the exception of the Parkinson’s Program, Sanofi Genzyme is required to pay an option exercise payment of \$20.0 million or \$30.0 million for each Split Territory Program and Spinal Muscular Atrophy Program.

Upon Sanofi Genzyme’s exercise of its option to license a given product in a Split Territory Program (“Split Territory Licensed Product”), the Company will have sole responsibility for the development of such Split Territory Licensed Product in the United States and Sanofi Genzyme shall have sole responsibility for development of such Split Territory Licensed Product in the rest of the world. The Company and Sanofi Genzyme will have shared responsibility for execution of ongoing development of such Split Territory Licensed Product that is not specific to either territory, including costs associated therewith. The Company is responsible for all commercialization activities relating to Split Territory Licensed Products in the United States, including all of the associated costs. Sanofi Genzyme is responsible for all commercialization activities relating to the Split Territory Licensed Products in the rest of the world, including all of the associated costs. If Sanofi Genzyme exercises its co-commercialization rights, Sanofi Genzyme will be the lead party responsible for all commercialization activities related to the Huntington’s Program product (the “Huntington’s Licensed Product”) in the United States.

Upon exercise of the option its option to license a product in the Spinal Muscular Atrophy Program (the “Spinal Muscular Atrophy Licensed Product”), Sanofi Genzyme shall have the sole right to develop the Spinal Muscular Atrophy Licensed Product worldwide. Sanofi Genzyme shall be responsible for all of the development costs that occur after the option exercise date for the Spinal Muscular Atrophy Program. Sanofi Genzyme is also responsible for worldwide commercialization activities relating to the Spinal Muscular Atrophy Licensed Product.

In October 2017, Sanofi Genzyme decided not to exercise its option for the Parkinson’s Program (the “PD Opt-Out”). Sanofi Genzyme is required to pay the Company for specified regulatory and commercial milestones, if achieved, up to \$540.0 million across all remaining programs. The Company is no longer entitled to receive a total of \$105.0 million related to regulatory and commercial milestone payments for the Parkinson’s Program as a result of the PD Opt-Out. The regulatory approval milestones are payable upon either regulatory approval in the United States or regulatory and reimbursement approval in the European Union and range from \$40.0 million to \$50.0 million per milestone, with an aggregate total of \$220.0 million, after accounting for the PD Opt-Out. The commercial milestones are payable upon achievement of specified annual net sales in each program and range from \$50.0 million to \$100.0 million per milestone, with an aggregate total of \$320.0 million, after accounting for the PD Opt-Out.

In addition, to the extent any Split Territory Licensed Products or the Spinal Muscular Atrophy Licensed Product are commercialized, the Company is entitled to tiered royalty payments ranging from the mid-single digits to mid-teens based on a percentage of net sales by Sanofi Genzyme. Sanofi Genzyme is entitled to receive tiered royalty payments related to sales of a Split Territory Licensed Product ranging from the low-single digits to mid-single digits based on a percentage of net sales by the Company depending on whether the Company uses Sanofi Genzyme technology in the Split Territory Licensed Product. If Sanofi Genzyme elects to co-commercialize the Huntington’s Licensed Product in the United States, the Company and Sanofi Genzyme will share in any profits or losses from Huntington’s Licensed Product sales.

The Sanofi Genzyme Collaboration Agreement will continue in effect until the later of (i) the expiration of the last to expire of the option rights and (ii) the expiration of all payment obligations unless sooner terminated by the Company or Sanofi Genzyme. The Company and Sanofi Genzyme have customary termination rights, including the right to terminate for an uncured material breach of the agreement committed by the other party and Sanofi Genzyme has the right to terminate for convenience.

Accounting Analysis

At inception, the Sanofi Genzyme Collaboration Agreement included the following performance obligations: (i) research and development services for each of the Split Territory Programs and the Spinal Muscular Atrophy Program, (ii) participation in the AJSC, (iii) participation in the DAC and (iv) a material right associated with an option to obtain a development and commercial license in the Parkinson’s Program (“PD Material Right”). The Company determined that the option to obtain a development and commercial license in the Parkinson’s Program was a material right under ASC 606 primarily because there were no additional option exercise payments payable by Sanofi Genzyme at the time of option exercise. Therefore, the PD Material Right was considered a performance obligation at the inception of the arrangement. The options in the other Split Territory Programs and the Spinal Muscular Atrophy Program do not provide a material right to the customer that it would receive without entering into the contract principally because the option fees are at least equal to the standalone selling price for the underlying goods. Therefore, the other Split Territory Programs and the Spinal Muscular Atrophy Program options are not performance obligations at inception.

The Company has identified \$74.6 million of total transaction price consisting of the \$65.0 million upfront fee, the \$5.0 million premium paid in excess of fair value of the Series B Preferred Stock and \$4.6 million of Sanofi Genzyme “in-kind” funding, which represents the transaction price at adoption. Additional consideration to be paid to the Company upon the exercise of the license options by Sanofi Genzyme or upon reaching certain milestones are excluded from the transaction price as they relate to option fees and milestones that can only be achieved subsequent to the option exercise or are outside of the initial contract term.

The Company has allocated the transaction price to the separate performance obligations based on their relative standalone selling price. For all performance obligations, the Company determined the standalone selling price at

contract inception estimated based on each obligation's estimated standalone selling price ("ESP"). The Company determined the ESP for the service related deliverable for the research and development activities based on internal estimates of the costs to perform the services, including expected internal expenses and expenses with third parties for services and supplies, marked up to include a reasonable profit margin and adjusted for the scope of the potential license. Significant inputs used to determine the total expense of the research and development activities include, the length of time required and the number and costs of various studies that will be performed to complete the applicable POP Study. The ESP for the AJSC and DAC have been estimated based on the costs incurred to participate in the committees, marked up to include a reasonable profit margin. The ESP for the PD Material Right was determined based on the estimated value of the license adjusted for the estimated probability that the option would be exercised by Sanofi Genzyme.

Based on the relative standalone selling price allocation, the allocation of the transaction price to the separate performance obligations was as follows:

<u>Performance Obligation</u>	<u>Amount</u> <u>(in thousands)</u>
Research and Development Services for:	
Huntington's Program	\$ 14,228
Parkinson's Program	6,040
Friedreich's Ataxia Program	14,821
Spinal Muscular Atrophy Program	29,116
Future Program	2,239
Committee Obligations:	
AJSC	133
DAC	207
PD Material Right	7,855
Total	\$ 74,639

The Company recognizes the amounts associated with research and development services and committee obligations on a proportional performance basis over the period of service using input-based measurements such as costs incurred to date, to estimate proportion performed, and remeasures its progress towards completion at the end of each reporting period. The amount allocated to the PD Material Right was initially deferred and recognized in full prior to the adoption of ASC 606.

During the three and six months ended June 30, 2018, the Company recognized \$0.7 million and \$1.2 million, respectively, of revenue associated with its collaboration with Sanofi Genzyme related to research and development services and committee obligations performed during the period. As of June 30, 2018, there was \$50.5 million of deferred revenue related to the Sanofi Genzyme Collaboration Agreement, which is classified as either current or noncurrent in the accompanying balance sheet based on the period the services are expected to be delivered.

Contingent consideration related to the performance of in-kind services is considered in the transaction price based on the most-likely amount, which is the full amount of the services that the Company can require Sanofi Genzyme to complete. There is no other available contingent consideration until such point as Sanofi Genzyme exercises an option to one of the research programs.

Costs incurred relating to the programs that Sanofi Genzyme has the option to license under the Sanofi Genzyme Collaboration Agreement consist of internal and external research and development costs, which primarily include: salaries and benefits, lab supplies and preclinical research studies. These costs are included in research and development expenses in the Company's statement of operations during the three and six months ended June 30, 2018 and 2017.

AbbVie Collaboration Agreement

Summary of Agreement

In February 2018, the Company entered into an exclusive collaboration and option agreement (the “AbbVie Collaboration Agreement”) with AbbVie Biotechnology Ltd (“AbbVie”) for the research, development and commercialization of AAV and other virus-based gene therapy products for the treatment of diseases of the central nervous system and other neurodegenerative diseases related to defective or excess aggregation of tau protein in the human brain, including Alzheimer’s disease. Under the AbbVie Collaboration Agreement, the Company and AbbVie have agreed to collaborate on the research and development of specified vectorized antibody compounds comprised of an AAV or other viral capsid and a virus vector genome that encodes one or more antibodies that target and bind to a tau protein. The collaboration is comprised of a research period (the “Research Period”), a development period (the “Development Period”), and an exclusive license option (the “License Option”). The AbbVie Collaboration Agreement included a non-refundable upfront payment of \$69.0 million for services during the Research Period.

During the Research Period, each party has agreed to identify up to five antibodies for inclusion in the collaboration. Subject to certain conditions and exceptions, the parties will select up to three antibodies (each, a “Research Antibody”) as candidates for creation of research compounds (each, a “Research Compound”), with AbbVie having the right to select two of the three Research Antibodies. The Company is required to use diligent efforts to conduct antibody engineering and other research activities to create Research Compounds and to develop product candidates containing or comprised of such Research Compounds (“Product Candidates”). The Company is solely responsible for its costs and expenses during the Research Period. During a specified portion of the Research Period, AbbVie may exercise one or more of its exclusive development options (each, a “Development Option”) to select up to a total of three Research Compounds (the “Selected Research Compounds”) and their corresponding Product Candidates (the “Selected Product Candidates”) to proceed to the Development Period.

Upon AbbVie’s exercise of a Development Option, AbbVie will pay the Company \$80.0 million for the first Selected Research Compound and \$30.0 million each for up to two additional Selected Research Compounds. During the Development Period, the Company is obligated to use diligent efforts to conduct development activities, including Investigational New Drug application-enabling and Phase 1 clinical trial activities, for the Selected Research Compounds and corresponding Selected Product Candidates. The Company will be solely responsible for the costs and expenses during the Development Period. During a specified portion of the Development Period (the “License Option Period”), AbbVie may exercise its License Option to further develop and commercialize all of the Research Compounds (the “Licensed Compounds”), and corresponding product candidates (the “Licensed Products”). Upon AbbVie’s exercise of its License Option, AbbVie will provide a one-time payment of \$75.0 million to the Company, and the Company will grant to AbbVie an exclusive, worldwide license, with the right to sublicense, under certain of the Company’s intellectual property rights to develop and commercialize the Licensed Compounds and the Licensed Products for all human diagnostic, prophylactic and therapeutic uses. In addition, after AbbVie’s exercise of the License Option, the Company has certain obligations to complete any remaining research and development activities that have not been completed for any Research Compounds and Product Candidates.

The Company’s research and development activities will be conducted pursuant to the plans agreed to by the parties and overseen by a joint governance committee (“JGC”) as detailed in the AbbVie Collaboration Agreement. Any material amendment to the research or development plans must be mutually agreed to by the Company and AbbVie, which may be through the JGC.

Under the AbbVie Collaboration Agreement, AbbVie is required to use commercially reasonable efforts to develop and commercialize at least one Licensed Product in each of the United States, Japan, the United Kingdom, Germany, France, Italy, and Spain. After exercise of the License Option, AbbVie is solely responsible for all development and commercialization activities relating to Licensed Compounds and Licensed Products at its sole cost and expense, subject to the agreed-upon research and development plans. The Company may elect to share in AbbVie’s development costs relating to a Licensed Product on an indication-by-indication basis in exchange for a specified increase in royalties (a “Cost-Sharing Option”). If the Company exercises a Cost-Sharing Option, the Company may either reimburse AbbVie for AbbVie’s applicable development costs or, in the case of certain budget overruns, AbbVie

may instead deduct applicable development costs, up to a specified cap, from milestone and royalty payments owed by AbbVie to the Company.

Under the AbbVie Collaboration, the Company is eligible to receive specified development and first-sale milestone payments for each Licensed Compound of up to an aggregate of \$550.0 million in the case of an Alzheimer's disease indication, up to \$230.0 million in the case of the first indication other than Alzheimer's disease and up to \$115.0 million for a subsequent non-Alzheimer's disease indication. Additionally, the Company is eligible to receive tiered, escalating royalties, in a range from a high-single digit to a mid-to-high teen (or, if the Company has exercised its Cost-Sharing Option, low-twenties) percentage of aggregate net sales of Licensed Products on a Licensed Compound by Licensed Compound basis, subject to potential reductions in certain circumstances. For each Licensed Product, AbbVie also has the right to decrease or eliminate its royalty payments on such Licensed Product in exchange for a one-time payment by AbbVie at a fair market value to be negotiated by the parties or determined pursuant to dispute resolution procedures specified in the AbbVie Collaboration Agreement.

Unless earlier terminated, the AbbVie Collaboration Agreement will expire on the earliest to occur of the expiration of (i) the Development Option Period, without AbbVie's exercise of a Development Option; (ii) the License Option Period, without AbbVie's exercise of its License Option; and (iii) the last-to-expire royalty term with respect to all Licensed Products in all countries. The Company and AbbVie have customary termination rights including the right to terminate for an uncured material breach of the agreement committed by the other party, and AbbVie has the right to terminate for convenience.

Accounting Analysis

The Company assessed the promised goods and services under the AbbVie Collaboration Agreement, in accordance with ASC 606, and determined that the AbbVie Collaboration Agreement includes the following performance obligations: (i) research services during the Research Period (through the delivery of the Final Research Report) including the identification of the Research Antibodies, conduct of research activities and provision of information to AbbVie to allow AbbVie to determine whether to exercise up to three Development Options to be rendered (collectively, the "Research Services"), and (ii) a material right associated with the Development Option on the first Research Compound and associated Product Candidates ("First Development Option Material Right"). The first Development Option provides AbbVie with (i) additional development services on a selected Research Compound and (ii) the ability to exercise the License Option. The Company has concluded the option provides a material right as the consideration paid by AbbVie upon exercise of the first Development Option is less than the amount that the Company would otherwise expect to receive outside the context of the contract.

The Company has concluded that the First Development Option Material Right is a separate performance obligation under ASC 606 as AbbVie is provided additional services and a License Option for additional consideration that represents a significant discount from amounts that would otherwise be offered outside the context of the contract. The First Development Option Material Right is distinct from the other performance obligations in the arrangement as it is an option in the contract that is not required for AbbVie to obtain the benefit of the other promised goods or services in the arrangement. The First Development Option Material Right does not include the underlying goods or services that are delivered upon exercise of the option, but rather represents the value to the customer of having the right to obtain development services and the right to the License Option at an advantageous price.

The Company received a nonrefundable, upfront payment of \$69.0 million as consideration under the AbbVie Collaboration Agreement, which represents the transaction price at inception. Additional consideration to be paid to the Company upon the exercise of the Development and License Options by AbbVie or upon reaching certain milestones are excluded from the transaction price as they relate to option fees and milestones that can only be achieved subsequent to the option exercise or are outside of the initial contract term.

The Company has allocated the transaction price to the separate performance obligations based on their relative standalone selling price. The Company determined the standalone selling price at contract inception based on each obligation's ESP. The Company determined the ESP for the research services obligation based on internal estimates of the costs to perform the services, including expected internal expenses and expenses with third parties for services and

supplies, inclusive of a reasonable profit margin. Significant inputs used to determine the total expense of the research services include the length of time required, the internal hours expected to be incurred on the services and the number and costs of various studies that will be performed to complete the Research Plan. The ESP for the First Development Option Material Right was determined based on the fees AbbVie would pay to exercise the Development and License Options, the estimated costs to perform the development services, inclusive of a reasonable profit margin, the estimated value of the License Option using comparable transactions, and the probability that the Development and License Options would be exercised by AbbVie.

Based on the relative standalone selling price, the allocation of the transaction price to the separate performance obligations was as follows:

Performance Obligation	Amount	
	(in thousands)	
Research Services	\$	34,482
First Development Option Material Right		34,518
Total	\$	69,000

The Company recognizes the amounts associated with Research Services on a proportional performance basis over the period of service using input-based measurements of total cost of research incurred to estimate proportion performed and remeasures its progress towards completion at the end of each reporting period. The amount allocated to the First Development Option Material Right is recorded as deferred revenue and will be recognized either over the period in which goods and services underlying the option are transferred or upon expiry of the option.

During the three and six months ended June 30, 2018, the Company recognized \$1.9 million and \$2.3 million, respectively, of revenue associated with the AbbVie Collaboration related to the Research Services performed during the period. As of June 30, 2018, there is \$66.7 million of deferred revenue related to the AbbVie Collaboration Agreement, which is classified as either current or noncurrent in the accompanying balance sheet based on the period the goods or services are expected to be delivered.

Costs incurred relating to the AbbVie Collaboration Agreement consist of internal and external research and development costs, which primarily include: salaries and benefits, lab supplies, and preclinical research studies. All of these costs are included in research and development expenses in the Company's statement of operations during the three and six months ended June 30, 2018.

MRI Interventions License and Securities Purchase Agreements

In September 2016, the Company entered into a securities purchase agreement (the "Securities Purchase Agreement") and a license agreement (the "MRIC License Agreement") with MRI Interventions, Inc. ("MRIC"). MRIC is the primary supplier of the ClearPoint® System, which is being used by the Company in ongoing development and clinical trials. Under the Securities Purchase Agreement, the Company paid \$2.0 million for shares of MRIC common stock and a warrant to purchase additional shares of MRIC common stock. The Company also entered into the MRIC License Agreement, which provided for certain rights to MRIC technology and for MRIC to transfer the rights and know-how to manufacture the ClearPoint System to enable the Company to utilize an alternative supplier for the ClearPoint System for use in the Company's development and clinical trials. During 2017, the Company terminated the MRIC License Agreement and all prior and future commitments and obligations under such agreement became null and void. The Company continues to hold the common stock and warrants to purchase additional shares of common stock as an available-for-sale security and non-current asset, respectively.

In May 2018, the Company entered into a master services and supply agreement with MRIC (the "MRIC Supply Agreement") which provides for MRIC to perform certain manufacturing, supply, development and services as requested by the Company, including the supply of the ClearPoint System and cannula devices. In both the three and six months ended June 30, 2018, the Company has incurred \$0.1 million of expense related to the MRIC Supply Agreement.

Other Agreements

During September 2016, the Company entered into a research and development funding arrangement with a non-profit organization that provides up to \$4.0 million in funding upon the achievement of clinical and development milestones. The agreement provides that the Company repay amounts received under certain circumstances including termination of the agreement, and to pay an amount up to 2.6 times the funding received upon successful development and commercialization of any products developed. During 2017, the Company earned a milestone payment of \$1.0 million. During the three and six months ended June 30, 2018, the Company did not earn any additional milestone payments. The Company has evaluated the arrangement and has concluded that it represents a research and development financing arrangement as it is probable that the Company will repay amounts received under the arrangement. As a result, the \$1.0 million earned to date is recorded as a non-current liability in the accompanying balance sheet.

Litigation

The Company is not a party to any legal matters and did not have contingency reserves established for any litigation liabilities as of June 30, 2018 or December 31, 2017.

7. Redeemable convertible preferred stock

The Company has authorized preferred stock amounting to 5,000,000 shares as of June 30, 2018 and December 31, 2017. The authorized preferred stock was classified under stockholders' equity at June 30, 2018 and December 31, 2017.

8. Stock-based compensation

2014 Stock Option and Grant Plan

In January 2014, the Company adopted the 2014 Stock Option and Grant Plan (the "2014 Plan"), under which it may grant incentive stock options, non-qualified stock options, restricted stock awards, unrestricted stock awards, or restricted stock units to purchase up to 823,529 shares of common stock to employees, officers, directors and consultants of the Company.

In April 2014, the Company amended the 2014 Plan to allow for the issuance of up to 1,411,764 shares of common stock. In August 2014, April 2015, August 2015, and October 2015, the Company further amended the 2014 Plan to allow for the issuance of up to 2,000,000, 2,047,058, 2,669,411, and 2,998,823 shares of common stock, respectively. During 2014 the Company issued only restricted stock awards under the 2014 Plan and during 2015 the Company only granted stock options under the 2014 Plan.

The terms of equity award agreements, including vesting requirements, are determined by the Board of Directors and are subject to the provisions of the 2014 Plan.

Founder Awards

In January 2014, the Company issued 1,188,233 shares of restricted stock to its founders at an original issuance price of \$0.0425 per share. Of the total restricted shares awarded to the founders, 835,292 shares generally vested over one to four years, based on each founder's continued service to the Company in varying capacity as a Scientific Advisory Board member, consultant, director, officer or employee, as set forth in each grantee's individual restricted stock purchase agreement.

The remaining 352,941 of the shares issued begin vesting upon the achievement of certain performance objectives as well as continued service to the Company, as set forth in the agreements. These performance conditions are tied to certain milestone events specific to the Company's corporate goals, including but not limited to preclinical and clinical development milestones related to the Company's product candidates. Stock-based compensation expense associated with these performance-based awards is recognized when the achievement of the performance condition is considered probable, using management's best estimates. During 2016, management determined that the achievement of

the performance milestone for one of the three performance-based awards had become probable and began recognizing stock-based compensation accordingly. The Company recorded \$0.1 million and \$0.3 million in stock-based compensation expense related to this award during the three and six months ended June 30, 2018, respectively. The Company recorded \$0.3 million and \$0.9 million in stock-based compensation expense related to this award during the three and six months ended June 30, 2017, respectively. No stock-based compensation expense was recorded for the remaining two founders' awards with performance-based vesting as of June 30, 2018 as the performance-based milestones related to these awards were not probable.

2015 Stock Option Plan

In October 2015, the Company's board of directors and stockholders approved the 2015 Stock Option and Incentive Plan (the "2015 Stock Option Plan") which became effective upon the completion of the IPO. The 2015 Stock Option Plan provides the Company with the flexibility to use various equity-based incentive and other awards as compensation tools to motivate its workforce. These tools include stock options, stock appreciation rights, restricted stock, restricted stock units, unrestricted stock, performance share awards and cash-based awards. The 2015 Stock Option Plan replaced the 2014 Plan. Any options or awards outstanding under the 2014 Plan remained outstanding and effective. The number of shares initially reserved for issuance under the 2015 Stock Option Plan is the sum of (i) 1,311,812 shares of common stock and (ii) the number of shares under the 2014 Plan that are not needed to fulfill the Company's obligations for awards issued under the 2014 Plan as a result of forfeiture, expiration, cancellation, termination or net issuances of awards thereunder. The number of shares of common stock that may be issued under the 2015 Stock Option Plan is also subject to increase on the first day of each fiscal year by up to 4% of the Company's issued and outstanding shares of common stock on the immediately preceding December 31.

Effective January 1, 2016, 2017, and 2018, an additional 1,069,971, 1,070,635, and 1,285,200 shares, respectively, were added to the Company's 2015 Stock Option Plan for future issuance. As of June 30, 2018, there were 2,026,589 shares of common stock available for future award grants under the 2015 Stock Option Plan. During the three and six months ended June 30, 2018, the Company issued a total of 258,100 and 1,184,191 stock options, respectively, to employees and directors under the 2015 Stock Option Plan. During the three and six months ended June 30, 2018, there were no new stock options issued to non-employees under the 2015 Stock Option Plan.

2015 Employee Stock Purchase Plan

In October 2015, the Company's board of directors and stockholders approved the 2015 Employee Stock Purchase Plan (the "2015 ESPP"). The 2015 ESPP became effective upon the closing of the IPO. Under the 2015 ESPP, all full-time employees of the Company are eligible to purchase common stock of the Company twice per year, at the end of each six-month payment period. During each payment period, eligible employees who so elect, may authorize payroll deductions in an amount of 1% to 10% (whole percentages only) of the employee's base pay for each payroll period. At the end of each payment period, the accumulated deductions are used to purchase shares of common stock from the Company at a discount. A total of 262,362 shares of common stock were initially authorized for issuance under this plan. The number of shares of common stock that may be issued under the 2015 ESPP is also subject to increase on the first day of each fiscal year by up to 1% of the Company's issued and outstanding shares of common stock on the immediately preceding December 31. Effective January 1, 2016, 2017, and 2018, 267,492, 267,658, and 321,300 shares of common stock, respectively, were added to the 2015 ESPP.

Stock-Based Compensation Expense

Total compensation cost recognized for all stock-based compensation awards in the statements of operations and comprehensive loss is as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
	(in thousands)			
Research and development	\$ 1,332	\$ 617	\$ 2,530	\$ 1,875
General and administrative	6,782	921	7,906	1,829
Total stock compensation expense	\$ 8,114	\$ 1,538	\$ 10,436	\$ 3,704

Restricted Stock

A summary of the status of and changes in unvested restricted stock activity under the Company's equity award plans for the six months ended June 30, 2018 was as follows:

	Shares	Weighted Average Grant Date Fair Value Per Share
Unvested restricted common stock as of December 31, 2017	557,979	\$ 0.70
Issued	—	—
Vested	(207,461)	\$ 0.87
Repurchased	(2,794)	\$ 1.11
Unvested restricted common stock as of June 30, 2018	<u>347,724</u>	<u>\$ 0.60</u>

The expense related to awards granted to employees and non-employees was \$46.5 thousand and \$0.1 million, respectively, for the three months ended June 30, 2018, and \$0.1 million and \$0.3 million for the six months ended June 30, 2018, respectively. The expense related to awards granted to employees and non-employees was \$0.1 million and \$29.0 thousand, respectively, for the three months ended June 30, 2017, and \$0.2 million and \$0.7 million for the six months ended June 30, 2017, respectively.

As of June 30, 2018, the Company had unrecognized stock-based compensation expense related to its unvested restricted stock awards of \$0.2 million, which is expected to be recognized over the remaining average vesting period of 0.1 years.

Stock Options

The following is a summary of stock option activity for the six months ended June 30, 2018:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2017	3,143,566	\$ 11.82		
Granted	1,184,191	\$ 23.88		
Exercised	(246,051)	\$ 10.27		
Cancelled or forfeited	(421,781)	\$ 15.42		
Outstanding at June 30, 2018	<u>3,659,925</u>	\$ 15.41	8.5	\$ 20,463
Exercisable at June 30, 2018	<u>1,245,966</u>	\$ 11.26	7.6	\$ 10,730
Vested and expected to vest at June 30, 2018	<u>3,659,925</u>	\$ 15.41	8.5	\$ 20,463

Using the Black-Scholes option pricing model, the weighted-average fair value of options granted to employees and directors during the three and six months ended June 30, 2018 was \$13.88 and \$15.92 per share, respectively. The expense related to options granted to employees and directors was \$7.9 million and \$9.8 million for the three and six months ended June 30, 2018, respectively. The weighted-average fair value of options granted to employees and directors during the three and six months ended June 30, 2017 was \$6.26 and \$7.55 per share, respectively. The expense related to awards granted to employees and directors was \$1.3 million and \$2.5 million for the three and six months ended June 30, 2017, respectively.

The fair value of each option issued to employees and directors was estimated at the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Risk-free interest rate	2.8 %	1.9 %	2.7 %	2.0 %
Expected dividend yield	— %	— %	— %	— %
Expected term (in years)	6.0	6.0	6.0	6.0
Expected volatility	74.7 %	75.9 %	74.4 %	74.0 %

There were no new options granted to non-employees during the three and six months ended June 30, 2018 and 2017. Unvested options granted to non-employees are revalued at each measurement period until fully vested. The expense related to stock option awards granted to non-employees was \$0.1 million and \$0.2 million for the three and six months ended June 30, 2018, respectively. The expense related to awards granted to non-employees was \$0.1 million and \$0.3 million for the three and six months ended June 30, 2017, respectively.

The fair value of each option issued to non-employees was estimated at each vesting and reporting date using the Black-Scholes option pricing model. The reporting date fair value was determined using the following weighted-average assumptions:

	As of June 30,	
	2018	2017
Risk-free interest rate	2.8 %	2.0 %
Expected dividend yield	— %	— %
Expected term (in years)	8.2	8.5
Expected volatility	74.4 %	78.4 %

As of June 30, 2018, the Company had unrecognized stock-based compensation expense related to its unvested stock options of \$22.5 million which is expected to be recognized over the remaining weighted-average vesting period of 2.7 years.

For the three and six months ended June 30, 2018 and 2017, due to a lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. In the three and six months ended June 30, 2018, the Company's estimate has also included the volatility of its common stock for the most recent period.

9. Income taxes

Deferred tax assets and deferred tax liabilities are recognized based on temporary differences between the financial reporting and tax basis of assets and liabilities using statutory rates. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized. Due to the uncertainty surrounding the realization of the favorable tax attributes in future tax returns, the Company has recorded a full valuation allowance against the Company's otherwise recognizable net deferred tax assets.

For the three and six months ended June 30, 2018, the Company recognized a de minimis tax expense in other comprehensive income related to the unrealized gain on available-for-sale securities. For the three and six months ended June 30, 2017, the Company recognized a tax expense in other comprehensive income of \$0.1 million related to the unrealized gain on available-for-sale securities.

10. Net loss per share

The following table sets forth the outstanding potentially dilutive securities that have been excluded in the calculation of diluted net loss per share because to include them would be anti-dilutive:

	As of June 30,	
	2018	2017
Unvested restricted common stock	347,724	863,435
Shares reserved for issuance under stock plans	6,700,282	2,844,555
Total	7,048,006	3,707,990

11. Related-party transactions

During the three and six months ended June 30, 2018 and 2017, the Company received consulting and management services from one of its investors. The total amount of consulting and management services provided by this investor was de minimis during the three and six months ended June 30, 2018 and 2017.

12. Subsequent events

Effective July 16, 2018, the Company appointed G. Andre Turenne as President and Chief Executive Officer. Mr. Turenne joins the Company from Sanofi Genzyme where he served most recently as Senior Vice President, Global Head, Business Development and Licensing since November 2015. Prior to his appointment to this role, Mr. Turenne held various other positions at Sanofi Genzyme including General Manager of Sanofi Genzyme Australia and New Zealand in 2015 and Vice President, Global Head of Genzyme Strategy and Business Development from 2011 to 2014. Prior to its acquisition by Sanofi Genzyme, Mr. Turenne served in several business development and commercial operations roles at Genzyme Corporation from 2006 to 2011. Mr. Turenne received a B.A. from Kalamazoo College and an M.B.A. from the Tuck School of Business at Dartmouth.

On July 16, 2018, in connection with the commencement of Mr. Turenne's employment, the Company issued to him a non-statutory stock option to purchase an aggregate of 650,000 shares of the Company's common stock at an exercise price of \$18.03 per share. Subject to Mr. Turenne's continued service to the Company, the stock option will vest over a four-year period, with 25% of the shares underlying the option award vesting on the first anniversary of the award and the remaining 75% of the shares underlying the award vesting monthly thereafter over the subsequent 36-month period. The stock option was issued outside of the Company's 2015 Stock Option Plan as an inducement material to Mr. Turenne's acceptance of an offer of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

Effective August 2, 2018, the Company entered into a consulting agreement (the "Paul Agreement") with Steven M. Paul, M.D., the Company's former President and Chief Executive Officer, pursuant to which Dr. Paul has agreed to provide consulting and advisory services, including but not limited to scientific guidance in connection with the certain of the Company's collaborations, research and development programs, and business development efforts, for a twelve-month period commencing on August 2, 2018. In accordance with its terms, the Paul Agreement may be extended at any time by mutual written consent of the parties or may be terminated by either party with cause; either party without cause, subject to forty-five-day notice; the mutual consent of the parties; or upon other specified conditions.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and the audited financial information and the notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2017, which was filed with the Securities and Exchange Commission, or the SEC, on March 14, 2018.

Our actual results and timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this Quarterly Report on Form 10-Q. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this Quarterly Report on Form 10-Q, they may not be predictive of results or developments in future periods.

The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Quarterly Report on Form 10-Q, including those risks identified under Part II, Item 1A. Risk Factors.

These forward-looking statements are made under the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements are neither promises nor guarantees. We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

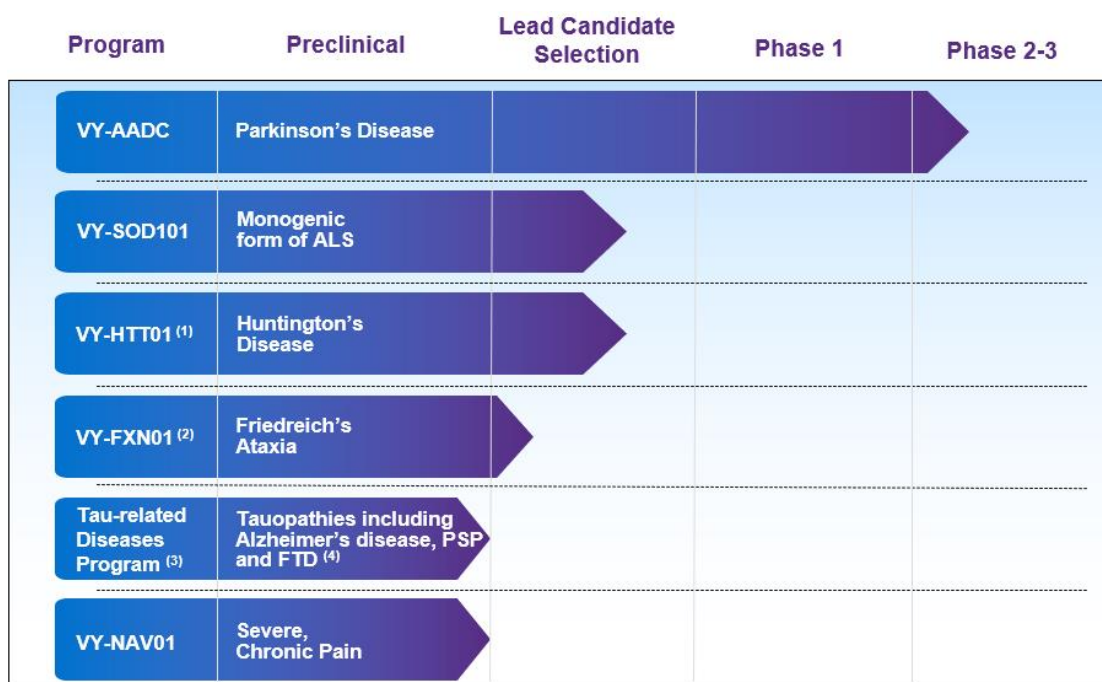
We are a clinical-stage gene therapy company focused on developing life-changing treatments for patients suffering from severe neurological diseases. We focus on neurological diseases where we believe an adeno-associated virus, or AAV, gene therapy approach that either increases or decreases the production of a specific protein can slow or reduce the symptoms experienced by patients, and therefore have a clinically meaningful impact. We have built a gene therapy platform that we believe positions us to be a leading company at the intersection of AAV gene therapy and severe neurological disease. Our gene therapy platform enables us to engineer, optimize, manufacture and deliver our AAV-based gene therapies that have the potential to provide durable efficacy following a single administration.

Additionally, we are working to identify novel AAV capsids, which are the outer viral protein shells that enclose the genetic material of the virus payload. Our team of experts in the fields of AAV gene therapy and neuroscience first identifies and selects severe neurological diseases that are well-suited for treatment using AAV gene therapy. We then engineer and optimize AAV vectors for delivery of the virus payload to the targeted tissue or cells. Our manufacturing process employs an established system that we believe will enable production of high quality AAV vectors at commercial-scale. Finally, we leverage established routes of administration and advances in dosing techniques to optimize delivery of our AAV gene therapies to target cells that are critical to the disease of interest, either directly to discrete regions of the brain, or, more broadly, to the spinal cord region.

Our business strategy focuses on discovering, developing, manufacturing and commercializing our gene therapy programs. As part of this strategy, we have developed core competencies specific to AAV gene therapy development and manufacturing and are beginning to build our commercial infrastructure. This business strategy also includes business development activities that may include in-licensing activities or partnering certain programs in certain geographies with collaborators, as we have demonstrated through our collaboration with Sanofi Genzyme, or the Sanofi Genzyme Collaboration, and our collaboration with AbbVie Biotechnology Ltd, or the AbbVie Collaboration. Since our inception,

our operations have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio, determining which neurological diseases to pursue, advancing our product candidates including delivery and manufacturing, and conducting preclinical studies and clinical trials. We do not have any product candidates approved for sale and have not generated any revenue from product sales. We have funded our operations primarily through private placements of redeemable convertible preferred stock, public offerings of our common stock, and the Sanofi Genzyme Collaboration, which commenced in February 2015 and the AbbVie Collaboration, which commenced in February 2018.

Our pipeline of gene therapy programs is summarized in the table below:



(1) Sanofi Genzyme has ex-U.S. options and option to co-promote in the U.S. (2) Sanofi Genzyme has ex-U.S. options (3) Tau program in collaboration with AbbVie (4) PSP = Progressive Supranuclear Palsy, FTD = Frontotemporal Dementia

Our pipeline consists of six programs for severe neurological indications, including Parkinson's disease; a monogenic form of amyotrophic lateral sclerosis, or ALS; Huntington's disease; Friedreich's ataxia; tau-related diseases including Alzheimer's disease, frontotemporal dementia, and progressive supranuclear palsy; and severe, chronic pain. We may seek orphan drug designation, breakthrough therapy designation, or other expedited review processes for our product candidates in the United States, Europe, and Japan.

Our most advanced clinical candidate, VY-AADC for the treatment of Parkinson's disease, is being evaluated in an open-label, Phase 1b clinical trial. Preliminary data from Cohorts 1 through 3 from this trial were reported beginning in late 2016 and most recently in March 2018. We have completed dosing patients in this Phase 1b clinical trial but continue to monitor their results. As discussed more fully in our most recent Annual Report on Form 10-K, the results of this Phase 1b clinical trial have demonstrated durable, dose-dependent and time-dependent improvements across multiple measures of patients' motor function at the timepoints reported after a one-time administration of the gene therapy. These measures include patient-reported diaries, Parkinson's disease rating scales, and quality of life, with diary on-time without troublesome dyskinesia at twelve months as the proposed primary endpoint of the pivotal program. Infusions of VY-AADC have been well-tolerated in all fifteen patients treated in these Cohorts with no reported vector-related serious adverse events, or SAEs. Fourteen of the 15 patients were discharged from the hospital within two days following surgery. As previously reported, one patient experienced two SAEs: a pulmonary embolism or blood clot in

the lungs, and related heart arrhythmia or irregular heartbeat. Investigators determined that these SAEs were most likely related to immobility during the administration of the product; consequently, deep vein thrombosis prophylaxis has been added to the clinical trial protocol.

In a separate Phase 1 clinical trial, we are also exploring a posterior, or back of the head, delivery approach of drug into the putamen, compared to a transfrontal, or top of the head, delivery approach used in Cohorts 1 through 3 of the ongoing Phase 1b clinical trial described above. During 2017, we dosed seven patients in this Phase 1 clinical trial designed to optimize the intracranial delivery of VY-AADC. In April 2018, we subsequently completed dosing an eighth patient. A posterior approach better aligns the infusion of VY-AADC with the anatomical structure of the putamen to potentially reduce the total procedure time and increase the total coverage of the putamen. Administration of VY-AADC with this posterior approach has been well-tolerated with no reported SAEs, with most patients discharged from the hospital the day after surgery. This trial utilized the same dose concentration as Cohort 3 of our Phase 1b clinical trial at a higher volume, yielding a total dose of up to 9.0×10^{12} vg compared with a total dose of up to 4.5×10^{12} vg in Cohort 3. As we announced in July 2018, interim results suggest that the posterior approach is associated with greater average putaminal coverage (approximately 50%), reduced total procedure times compared with the transfrontal approach of Cohorts 1 through 3 used in the Phase 1 clinical trial by two to three hours, and improvements in patients' motor function at six months, which were consistent with improvements achieved from patients in Cohorts 2 and 3 at the same time point in our Phase 1b trial with VY-AADC.

In June 2018, the U.S. Food and Drug Administration, or FDA, granted Regenerative Medicine Advance Therapy, or RMAT, designation for our VY-AADC gene therapy treatment. The designation was based on our Phase 1b clinical data with VY-AADC. Previously, the FDA also granted fast-track designation to VY-AADC. Additionally, in July 2018, we received feedback from a Type C meeting with the FDA. Based on the written response from the FDA, we are continuing to plan to submit for review a biologics license application, or BLA, for VY-AADC based on the nonclinical and clinical safety and efficacy data from the pivotal program, including data from the randomized, placebo-controlled Phase 2 trial alone, or if needed, from the planned randomized, placebo-controlled Phase 3 trial.

Informed by the results of the Phase 1 clinical trials, we have determined that the posterior approach is the preferred surgical route of administration for the pivotal Phase 2-3 clinical program. For the pivotal Phase 2 trial, we have selected a dose of up to 2.5×10^{12} vector genomes, which is defined as a maximum total bilateral dose. This dose is between the up to maximum total vector genome doses administered in Cohorts 2 and 3 from the Phase 1b trial when considering the higher volume administered with the posterior trajectory and vector produced using the baculovirus system.

The Phase 2 trial is a randomized, placebo-controlled trial with a planned enrollment of up to 42 patients who have been diagnosed with Parkinson's disease for at least four years. Patients will be randomized 1:1 to either VY-AADC or placebo surgery. After treatment with either VY-AADC or placebo surgery, patients will be followed in a blinded manner for 12 months, at which point, the trial will unblind, and safety and efficacy measures will be assessed. The primary efficacy endpoint of the trial is the improvement from baseline to 12 months in a patient's self-reported diary on-time without troublesome dyskinesia in the VY-AADC treatment arm compared to the placebo surgery arm. Multiple secondary endpoints include the assessment of other motor function from patient diaries as well as assessments from the United Parkinson's Disease Rating Scale (UPDRS) scores, including UPDRS-3 and UPDRS-2 scores. The Phase 2 trial is 80% powered to detect a 2.0 hour improvement in the primary endpoint of diary on-time without troublesome dyskinesia from baseline to twelve months for the treatment arm compared with the placebo arm. Clinical trial sites for the Phase 2 portion of the pivotal program have been identified with institutional review board submission and site activation underway. We anticipate the trial to take approximately one year to enroll. During the remainder of the year, we plan to provide updates as to the enrollment status of the Phase 2 trial.

We are pursuing additional product candidates in the preclinical stages of development, including treatment programs for ALS, Huntington's disease, Friedreich's ataxia, tau-related neurodegenerative diseases and the treatment of severe, chronic pain. We plan to file INDs from our ALS and Huntington's disease programs during 2019. In late 2017, we initiated additional preclinical studies to further optimize our ALS program's therapeutic approach, including exploration of additional routes of administration and novel AAV capsids in large animal models. We selected VY-HTT01 as our clinical candidate for the treatment of Huntington's disease and further optimization of routes of

administration is underway to support filing of a potential IND application. Additional preclinical studies are underway including steps to optimize a lead clinical candidate for the treatment of Friedrich's ataxia. In February 2018, we announced a global, strategic collaboration with AbbVie to develop potential new gene therapies consisting of vectors to deliver monoclonal antibodies to the brain directed against tau for Alzheimer's disease and other tau-related neurodegenerative diseases. We are conducting proof-of-concept studies on our VY-NAV01 program for the treatment of severe, chronic pain. Additionally, we continue to evaluate additional severe neurological diseases that could be treated using AAV gene therapy through application of either a gene replacement or a gene knockdown approach. Beyond these approaches, we are also actively exploring additional potential treatment methods that can utilize an AAV vector, including gene editing to correct or delete a gene in the cell genome.

Finally, we are also developing our own real-time, intra-operative, magnetic resonance imaging, or MRI, compatible device, the trajectory array guide device, that can be used with other neuro-navigational systems for the administration of drug to the putamen and other surgical procedures to avoid blood vessels and reduce the risk of potential hemorrhage during surgery and to maximize drug coverage of the putamen. In July 2018, the Center for Devices and Radiological Health of the FDA provided 510(k) clearance for the trajectory array guide device. Investigators have used an alternative MRI-compatible device called the ClearPoint® System in our Phase 1b clinical trial of VY-AADC and Phase 1 posterior trajectory trial.

We have incurred significant operating losses since our inception. Our net losses were \$45.5 million for the six months ended June 30, 2018. As of June 30, 2018, we had an accumulated deficit of \$226.2 million, which included a \$20.0 million cumulative catch-up adjustment related to the adoption of ASC 606, *Revenue from Contracts with Customers*, or ASC 606. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase significantly in connection with our ongoing activities, if and as we:

- continue investing in our gene therapy platform to optimize vector engineering, manufacturing and dosing and delivery techniques;
- continue to advance our clinical candidate, VY-AADC, through the ongoing Phase 1b clinical trial and into the pivotal Phase 2-3 clinical program as a treatment for Parkinson's disease;
- initiate additional preclinical studies and clinical trials for, and continue research and development of, our other programs;
- conduct joint research and development under the AbbVie Collaboration for the research, development, and commercialization of AAV and other virus-based gene therapy products for the treatment of diseases of the central nervous system and other neurodegenerative diseases related to defective or excess aggregation of tau protein in the human brain, including Alzheimer's disease;
- continue our process research and development activities, as well as establish our research-grade and commercial manufacturing capabilities;
- identify additional neurological diseases for treatment with our AAV gene therapies and develop additional programs or product candidates;
- work to identify and optimize novel AAV capsids;
- develop, obtain and maintain regulatory clearances for devices to deliver our AAV gene therapies;
- seek marketing and regulatory approvals for VY-AADC or other product candidates or devices that arise from our programs that successfully complete clinical development;
- maintain, expand and protect our intellectual property portfolio;

- identify, acquire or in-license other product candidates and technologies;
- develop a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- expand our operational, financial and management systems and personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- increase our product liability and clinical trial insurance coverage as we expand our clinical trials and commercialization efforts; and
- continue to operate as a public company.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the foreseeable future. For the six months ended June 30, 2018, we recognized \$1.2 million of collaboration revenue from the Sanofi Genzyme Collaboration and \$2.3 million of collaboration revenue from the AbbVie Collaboration. For additional information about our revenue recognition policy related to collaborations, see the section titled “—Critical Accounting Policies and Estimates—Revenue.”

For the foreseeable future, we expect substantially all of our revenue will be generated from our collaborations with Sanofi Genzyme and AbbVie, and any other strategic relationships we may enter into. If our development efforts are successful, we may also generate revenue from product sales.

Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our program discovery efforts, and the development of our programs and gene therapy platform, which include:

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- costs of funding research performed by third parties that conduct research and development, preclinical activities, manufacturing and production design on our behalf;
- the cost of purchasing lab supplies and non-capital equipment used in designing, developing and manufacturing preclinical study materials;
- consultant fees;
- facility costs including rent, depreciation and maintenance expenses; and
- fees for maintaining licenses under our third-party licensing agreements.

Research and development costs are expensed as incurred. Costs for certain activities, such as manufacturing, preclinical studies, and clinical trials, are generally recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and collaborators.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales of our product candidates. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty of:

- successful enrollment in and completion of clinical trials;
- establishing an appropriate safety profile;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- receipt of marketing approvals from applicable regulatory authorities;
- commercializing the product candidates, if and when approved, whether alone or in collaboration with others;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- maintaining acceptable safety profiles of the products following approval; and
- retaining key research and development personnel.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate.

Research and development activities are central to our business model. We expect research and development costs to increase significantly for the foreseeable future as our development programs progress, including as we continue to support the Phase 1b clinical trial and initiate the pivotal Phase 2-3 clinical trial program of VY-AADC as a treatment for Parkinson's disease, and move such product candidates into additional clinical trials. Additionally, we expect research and development costs associated with activities under the AbbVie Collaboration to increase as our efforts on the tau-related diseases program expand. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, business development, legal and human resource functions. Other significant costs include corporate facility costs not otherwise included in research and development expenses, legal fees related to patent and corporate matters and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, including the pivotal Phase 2-3 program of VY-AADC, the expanded efforts on the tau-related diseases program in connection with the AbbVie Collaboration, and the initiation of clinical trials for our other product candidates. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants. We also anticipate increased expenses associated with being a public company, including costs for audit, legal, regulatory, and tax-related services, director and officer insurance premiums, business development activities, and investor relations costs.

Critical Accounting Policies and Estimates

See “*Recently Adopted Accounting Pronouncements*” below for discussion of our adoption of new revenue recognition guidance using the modified retrospective method as of January 1, 2018. All amounts and disclosures set forth in this Management’s Discussion and Analysis of Financial Condition and Results of Operations reflect these changes.

We have prepared our financial statements in accordance with U.S. generally accepted accounting principles. Our preparation of these financial statements requires us to make estimates, assumptions, and judgments that affect the reported amounts of assets, liabilities, expenses, and related disclosures at the date of the financial statements, as well as revenue and expenses recorded during the reporting periods. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results could therefore differ materially from these estimates under different assumptions or conditions.

Effective January 1, 2018, we adopted the provisions of ASC 606 using the modified retrospective transition method. Under this method, we recorded the cumulative effect of initially applying the new standard to all contracts as of the date of adoption.

We enter into collaboration agreements which are within the scope of ASC 606, under which we license rights to certain of our product candidates and perform research and development services. The terms of these arrangements typically include payment of one or more of the following: non-refundable, upfront fees; reimbursement of research and development costs; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, we perform the following five steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. We only apply the five-step model to contracts when it is probable that we will collect consideration we are entitled to in exchange for the goods or services we transfer to the customer.

The promised good or services in our arrangement typically consist of license rights to our intellectual property or research and development services. We provide options to additional items in the contracts, which are accounted for as separate contracts when the customer elects to exercise such options, unless the option provides a material right to the customer. We evaluate the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer and are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised good or services are distinct, we consider factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on their own or whether the required expertise is readily available and whether the goods or services are integral or dependent to other goods or services in the contract.

We estimate the transaction price based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration may include fixed consideration or variable consideration. At the inception of each arrangement that includes variable consideration, we evaluate the amount of potential payment and the likelihood that the payments will be received. We utilize either the most likely amount method or expected amount

method to estimate the amount expected to be received based on which method best predicts the amount expected to be received. The amount of variable consideration which is included in the transaction price may be constrained, and is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period.

Our contracts often include development and regulatory milestone payments which are assessed under the most likely amount method and constrained if it is probable that a significant revenue reversal would occur. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues in the period of adjustment. To date, we have not recognized any consideration related to the achievement of development, regulatory, or commercial milestone revenue resulting from any of our collaboration arrangements.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any consideration related to sales-based royalty revenue resulting from any of our collaboration arrangements.

We allocate the transaction price based on the estimated stand-alone selling price of each of the performance obligations. We must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. We utilize key assumptions to determine the stand-alone selling price for service obligations, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. Additionally, in determining the standalone selling price for material rights, we utilize comparable transactions, industry standards for product development and clinical trial success probabilities and estimates of option exercise likelihood. Variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated are consistent with the amounts we would expect to receive for the satisfaction of each performance obligation.

The consideration allocated to each performance obligation is recognized as revenue when control is transferred for the related goods or services. For performance obligations which consist of licenses and other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Upfront payments and fees are recorded as deferred revenue upon receipt or when due until we perform our obligations under these arrangements. Amounts are recorded as accounts receivable when our rights to consideration are unconditional.

Recently Adopted Accounting Pronouncements

In January 2016, the Financial Accounting Standard Board, or FASB, issued ASC Update No. 2016-01, *Financial Instruments - Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities*. The purpose of Update No. 2016-01 is to improve financial reporting for financial instruments by reducing the number of items recorded to other comprehensive income. We adopted Update No. 2016-01 in the first quarter of 2018, using the modified retrospective method. Unrealized gains and losses previously recorded to other comprehensive income (loss) were reclassified to accumulated deficit and all future fair value changes will be recorded to other income (loss). The adoption of the standard on January 1, 2018 did not have a material impact on our consolidated financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows*, or ASC 230, which simplifies certain elements of cash flow classification. The new guidance is intended to reduce diversity in practice in how certain transactions are classified in the statement of cash flows. The new guidance will be effective for annual periods beginning after December 15, 2017. The adoption of ASC 230 on January 1, 2018 did not have a material impact on our consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash*, or ASU 2016-18. The amendments in ASU 2016-18 require an entity to reconcile and explain the period-over-period change in total cash, cash equivalents and restricted cash within its statements of cash flows and was applied utilizing a full retrospective approach. We adopted the new standard on January 1, 2018. We have included the necessary reconciliation within Note 4 “Cash, cash equivalents, restricted cash, and available for sale marketable securities” of the notes to our unaudited condensed consolidated financial statements appearing elsewhere in this Quarterly Report on Form 10-Q.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers*, or ASU 2014-09, which supersedes the revenue recognition requirements in ASC 605, *Revenue Recognition*, or ASC 605, and most industry-specific guidance. The new standard requires that an entity recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The update also requires additional disclosure about the nature, amount, timing, and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. Thereafter, a series of clarifying ASU’s, narrow scope improvements and practical expedients were issued. This collective guidance resulted in the new revenue standards; ASC 606. ASC 606 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017 and should be applied retrospectively to each prior reporting period presented or retrospectively with the cumulative effect of initially applying this update recognized at the date of initial application.

We adopted the new standard effective January 1, 2018 using the modified retrospective approach. We had one open contract, with Sanofi Genzyme, on the adoption date and have assessed it under the new revenue standard. The adoption of ASC 606 resulted in the changes to (i) the allocation of arrangement consideration, including the determination of estimated selling price and the allocation of variable consideration to specific performance obligations and (ii) the application of proportional performance as a measure of progress on service related deliverables.

We have accounted for the impact of adopting ASC 606 as a cumulative catch-up under the modified retrospective approach, which represented as an increase of \$20.0 million to deferred revenue with an offset to accumulated deficit, effective January 1, 2018. The following financial statement line items have been shown to reflect comparative balances under ASC 606 and ASC 605 for each of the three-month period and six-month period ended June 30, 2018 for both the Sanofi Genzyme Collaboration and AbbVie Collaboration, collectively.

Condensed Consolidated Statements of Operations and Comprehensive Loss

	Three months ended June 30, 2018		
	Under ASC 606	Under ASC 605	Effect of change
	(in thousands, except per share data)		
Collaboration revenue	\$ 2,575	\$ 2,908	\$ (333)
Loss before income taxes	(25,541)	(25,208)	(333)
Net loss	(25,541)	(25,208)	(333)
Net loss per share, basic and diluted	(0.80)	(0.79)	(0.01)

	Six months ended June 30, 2018		
	Under ASC 606	Under ASC 605	Effect of change
	(in thousands, except per share data)		
Collaboration revenue	\$ 3,517	\$ 4,213	\$ (696)
Loss before income taxes	(45,648)	(44,952)	(696)
Net loss	(45,468)	(44,772)	(696)
Net loss per share, basic and diluted	(1.43)	(1.40)	(0.03)

Condensed Consolidated Balance Sheets

	As of June 30, 2018		
	Under ASC 606	Under ASC 605	Effect of change
	(in thousands)		
Deferred revenue, current	\$ 19,840	\$ 17,819	\$ 2,021
Deferred revenue, non-current	97,308	78,703	18,605
Accumulated deficit	(226,231)	(205,605)	(20,626)

Condensed Consolidated Statements of Cash Flows

	Six months ended June 30, 2018		
	Under ASC 606	Under ASC 605	Effect of change
	(in thousands)		
Net loss	\$ (45,468)	\$ (44,772)	\$ (696)
Adjustments to reconcile net loss to net cash provided by operating activities:			
Deferred revenue	65,482	64,786	696

Results of Operations

Comparison of the three months ended June 30, 2018 and 2017

The following table summarizes our results of operations for the three months ended June 30, 2018 and 2017, together with the changes in those items in dollars:

	Three Months Ended		
	June 30,		Change
	2018	2017	
	(in thousands)		
Collaboration revenue	\$ 2,575	\$ 1,177	\$ 1,398
Operating expenses:			
Research and development	16,507	15,300	1,207
General and administrative	11,762	4,516	7,246
Total operating expenses	28,269	19,816	8,453
Other income (expense), net:			
Interest income	870	255	615
Other expense	(717)	(297)	(420)
Total other income (expense), net	153	(42)	195
Loss before income taxes	(25,541)	(18,681)	(6,860)
Income tax provision	—	(195)	195
Net loss	\$ (25,541)	\$ (18,876)	\$ (6,665)

Collaboration Revenue

Collaboration revenue was \$2.6 million and \$1.2 million for the three months ended June 30, 2018 and 2017, respectively. During the three months ended June 30, 2018, collaboration revenue included amounts related to the Sanofi Genzyme Collaboration, in addition to research services related to the AbbVie Collaboration. The increase in revenue is a result of \$1.9 million related to the AbbVie Collaboration which we entered into in February 2018, offset by a reduction of \$0.5 million related to the adoption of ASC 606, effective January 1, 2018. The most significant changes to revenue recognition was the adoption of a proportional performance basis for estimating progress to completion of research and development services under each program of the Sanofi Genzyme Collaboration.

During the three months ended June 30, 2017, collaboration revenue was comprised of amounts recognized for research and development services for various programs under the Sanofi Genzyme Collaboration.

Research and Development Expense

Research and development expense increased by \$1.2 million from \$15.3 million for the three months ended June 30, 2017, to \$16.5 million for the three months ended June 30, 2018. The following table summarizes our research and development expenses for the three months ended June 30, 2018 and 2017, together with the change in those items in dollars:

	Three Months Ended		
	June 30,		Change
	2018	2017	
	(in thousands)		
External research and development expenses	\$ 7,768	\$ 8,299	\$ (531)
Employee and contractor related expenses	6,318	4,800	1,518
Facility and other expenses	2,207	1,886	321
License fees	214	315	(101)
Total research and development expenses	<u>\$ 16,507</u>	<u>\$ 15,300</u>	<u>\$ 1,207</u>

The increase in research and development expense for the three months ended June 30, 2018 was primarily attributable to the following:

- approximately \$1.5 million for increased research and development employee-related and consultant compensation costs as we continue to increase research and development headcount;
- approximately \$0.3 million increased facility and other costs including rent, depreciation, maintenance and other expenses due to the additional space leased at 64 Sidney Street and 75 Sidney Street;
- offset by approximately \$0.5 million for decreased external research and development costs due to manufacturing and the timing of major studies; and
- approximately \$0.1 million for decreased intellectual property and license fees.

General and Administrative Expense

General and administrative expense increased by \$7.2 million from \$4.5 million for the three months ended June 30, 2017 to \$11.7 million for the three months ended June 30, 2018. The increase in general and administrative expense was primarily attributable to the following:

- approximately \$6.3 million for increased employee compensation cost due to increases in headcount and stock-based compensation, which included the one-time recognition of \$5.4 million of stock-based compensation related to Dr. Paul's retirement agreement;
- approximately \$0.9 million for increased legal and intellectual property expenses; and
- approximately \$0.1 million for increased facility and other costs including rent, depreciation, maintenance and other expenses.

Other Income, net

Interest income of approximately \$0.9 million was recognized during the three months ended June 30, 2018 related to our marketable securities balances. The balance was offset by a \$0.7 million loss related to our investment in common stock and warrants to purchase shares of common stock of MRI Interventions, Inc., or MRIC.

Interest income of approximately \$0.3 million was recognized during the three months ended June 30, 2017 related to from our marketable securities balances. The balance was offset by a \$0.3 million net loss related to mark-to-market losses recognized on the fair value of warrants to purchase equity securities.

Comparison of the six months ended June 30, 2018 and 2017

The following table summarizes our results of operations for the six months ended June 30, 2018 and 2017, together with the changes in those items in dollars:

	Six Months Ended		Change
	June 30,		
	2018	2017	
	(in thousands)		
Collaboration revenue	\$ 3,517	\$ 2,642	\$ 875
Operating expenses:			
Research and development	31,360	29,372	1,988
General and administrative	18,945	9,430	9,515
Total operating expenses	<u>50,305</u>	<u>38,802</u>	<u>11,503</u>
Other income, net:			
Interest income	1,458	508	950
Other (expense) income	(318)	98	(416)
Total other income, net	<u>1,140</u>	<u>606</u>	<u>534</u>
Loss before income taxes	(45,648)	(35,554)	(10,094)
Income tax benefit	180	31	149
Net loss	<u>\$ (45,468)</u>	<u>\$ (35,523)</u>	<u>\$ (9,945)</u>

Collaboration Revenue

Collaboration revenue was \$3.5 million and \$2.6 million for the six months ended June 30, 2018 and 2017, respectively. During the six months ended June 30, 2018, collaboration revenue included amounts related to the Sanofi Genzyme Collaboration in addition to research services related to the AbbVie Collaboration. The increase in revenue is a

result of \$2.3 million related to the AbbVie Collaboration which we entered into in February 2018, offset by a reduction of \$1.4 million of amounts related to the Sanofi Genzyme Collaboration. In 2017, we fully recognized all amounts related to the Parkinson's program. Additionally, we adopted ASC 606, effective January 1, 2018. The most significant change to revenue recognition is the adoption of a proportional performance basis for estimating progress to completion of research and development services under each program of the Sanofi Genzyme Collaboration.

During the six months ended June 30, 2017, collaboration revenue was comprised of amounts recognized for research and development services for various programs under the Sanofi Genzyme Collaboration.

Research and Development Expense

Research and development expense increased by \$2.0 million from \$29.4 million for the six months ended June 30, 2017, to \$31.4 million for the six months ended June 30, 2018. The following table summarizes our research and development expenses, for the six months ended June 30, 2018 and 2017:

	Six Months Ended		Change
	June 30,		
	2018	2017	
	(in thousands)		
External research and development expenses	\$ 14,790	\$ 15,342	\$ (552)
Employee and contractor related expenses	12,110	10,048	2,062
Facility and other expenses	4,088	3,651	437
License fees	372	331	41
Total research and development expenses	\$ 31,360	\$ 29,372	\$ 1,988

The increase in research and development expense for the six months ended June 30, 2018 was primarily attributable to the following:

- approximately \$2.1 million for increased research and development employee-related and consultant compensation costs as we continue to increase research and development headcount;
- approximately \$0.4 million increased facility and other costs including rent, depreciation, maintenance and other expenses due to the additional space leased at 64 Sidney Street and 75 Sidney Street;
- offset by approximately \$0.6 million for decreased external research and development costs due to manufacturing and the timing of major studies.

General and Administrative Expense

General and administrative expense increased by \$9.5 million from \$9.4 million for the six months ended June 30, 2017 to \$18.9 million for the six months ended June 30, 2018. The increase in general and administrative expense was primarily attributable to the following:

- approximately \$7.5 million for increased employee compensation cost due to increases in headcount and stock-based compensation, which included the one-time recognition of \$5.4 million of stock-based compensation related to Dr. Paul's retirement agreement;
- approximately \$1.7 million for increased legal and intellectual property expenses; and
- approximately \$0.3 million for increased facility and other costs including rent, depreciation, maintenance and other expenses.

Other Income, net

Interest income of approximately \$1.5 million was recognized during the six months ended June 30, 2018 related to our marketable securities balances. The balance was offset by a \$0.3 million loss related to our investment in common stock and warrants to purchase shares of common stock of MRI Interventions, Inc., or MRIC.

Other income of approximately \$0.1 million was recognized during the six months ended June 30, 2017 related to grants received. There was approximately \$0.5 million of interest income due to our marketable securities balances during the six months ended June 30, 2017.

Liquidity and Capital Resources*Sources of Liquidity*

We have funded our operations primarily through private placements of redeemable convertible preferred stock, public offerings of our common stock, and the Sanofi Genzyme Collaboration which commenced in February 2015 and the AbbVie Collaboration which commenced in February 2018.

On November 16, 2015, we closed our initial public offering, or IPO, whereby we sold 5,750,000 shares of common stock, at a public offering price of \$14.00 per share, including 750,000 shares of common stock issued upon the full exercise by the underwriters of their option to purchase additional shares, resulting in net proceeds to us of \$72.9 million after deducting underwriting discounts and commissions and offering expenses payable by us. On November 7, 2017, we sold 5,175,000 shares of common stock to the public at an offering price of \$12.00 per share, including 675,000 shares of common stock issued upon the full exercise by the underwriters of their option to purchase additional shares, resulting in net proceeds to us of \$58.0 million after deducting underwriting discounts, commissions, and offering expenses payable by us.

As of June 30, 2018, we had cash, cash equivalents, and marketable debt securities of \$197.0 million.

Cash Flows

The following table provides information regarding our cash flows for the six months ended June 30, 2018 and 2017:

	Six Months Ended	
	June 30,	
	2018	2017
	(in thousands)	
Net cash provided by (used in):		
Operating activities	\$ 26,108	\$ (30,629)
Investing activities	(970)	59,188
Financing activities	2,946	1,100
Net increase in cash, cash equivalents, and restricted cash	\$ 28,084	\$ 29,659

Net Cash Provided by (Used in) Operating Activities

Net cash provided by operating activities was \$26.1 million during the six months ended June 30, 2018 compared to \$30.6 million of cash used in operating activities during the six months ended June 30, 2017. The increase in cash provided by operating activities is primarily due to the receipt of \$69.0 million related to the AbbVie Collaboration, offset by increases in operating expenses due to increased research and development activities, as well as higher general and administrative expenses as a result of a higher headcount, legal fees, and stock-based compensation year over year.

Net Cash (Used in) Provided by Investing Activities

Net cash used in investing activities was \$1.0 million during the six months ended June 30, 2018 compared to \$59.2 million of cash provided by investing activities during the six months ended June 30, 2017. The increase in cash used in investing activities for the six months ended June 30, 2018 was primarily due to purchases of \$205.0 million of marketable securities and \$3.0 million for purchases of property and equipment, offset by \$207.0 million of proceeds from maturities of marketable securities. The cash provided by investing activities for the six months ended June 30, 2017 was primarily due to proceeds from maturities of marketable securities of \$62.6 million, offset by \$3.6 million for purchases of marketable securities.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was \$2.9 million and \$1.1 million during the six months ended June 30, 2018 and 2017, respectively, primarily from proceeds of exercises of stock options.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue or initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant expenses related to program sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of potential collaborators. Furthermore, we expect to incur additional costs associated with 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 or enter into business development transactions when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Based upon our current operating plan, we expect our existing cash, cash equivalents, and marketable debt securities will enable us to fund our operating expenses and capital expenditure requirements into early 2020. Our future capital requirements will depend on many factors, including:

- the scope, progress, results, and costs of product discovery, preclinical studies and clinical trials for our product candidates and any required companion devices;
- the scope, progress, results, costs, prioritization, and number of our research and development programs;
- the progress and status of the Sanofi Genzyme collaboration and the AbbVie Collaboration, including any research and development costs for which we are responsible, the potential exercise by our collaboration partners of options to develop or license certain products and product candidates, and our potential receipt of future milestone payments and royalties from our collaboration partners;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, preclinical development and clinical trial costs, or the achievement of milestones or occurrence of other developments that trigger payments, under any other collaboration agreement to which we might become a party;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaboration, distribution, or other marketing arrangements for our product candidates on favorable terms, if at all;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;

- the extent to which we acquire or in-license other product candidates and technologies or acquire or invest in other businesses, such as our investment in MRI Interventions, Inc.;
- the costs related to evaluating possible alternative devices that may be useful in the delivery of our product candidates, including our ongoing development of our trajectory array guide device;
- the costs of securing manufacturing arrangements for pre-commercial and commercial production;
- the level of product sales from any product candidates for which we obtain marketing approval in the future; and
- the costs of establishing or contracting for sales, manufacturing, marketing, distribution, and other commercialization capabilities if we obtain regulatory approvals to market our product candidates.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete. We may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenues, if any, and any commercial milestones or royalty payments under our collaboration agreements, will be derived from sales of products that may not be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing and business development transactions to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate product revenues sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or equity-linked securities, including convertible debt, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our existing stockholders' rights as holders of our common stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, obtaining additional capital, acquiring or divesting businesses, making capital expenditures or declaring dividends.

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

Contractual Obligations

The following table summarizes our significant contractual obligations as of payment due date by period at June 30, 2018:

	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
Operating lease commitments ⁽¹⁾	\$ 42,954	\$ 2,110	\$ 9,056	\$ 9,864	\$ 21,924

(1) We lease office space at 75 Sidney Street and 64 Sidney Street in Cambridge, Massachusetts under non-cancelable operating leases that expire in December 2026.

In February 2018, we executed a second amendment for additional space located at 75 Sidney Street in Cambridge, Massachusetts, concurrent to the existing leases with terms going through December 2024. In June 2018, we executed a third amendment for additional space located at 75 Sidney Street, including an extension to the term through

November 2026. Additionally, we executed an amendment to the lease at 64 Sidney Street to extend the term through November 2026.

We enter into agreements in the normal course of business with clinical research organizations, contract manufacturing organizations, and institutions to license intellectual property. We have not included these future payments in the table of contractual obligations above since the contracts are cancelable at any time by us, generally upon 30 to 90 days prior written notice.

In February 2015, we entered into an agreement in connection with the Sanofi Genzyme Collaboration, or the Sanofi Genzyme Collaboration Agreement, pursuant to which we granted Sanofi Genzyme an exclusive option to license, develop, and commercialize (i) ex-U.S. rights to several programs including our programs for Parkinson's disease and Friedreich's Ataxia, (ii) ex-U.S. rights and U.S. co-commercialization rights to our program for Huntington's disease, and (iii) worldwide rights to our program for Spinal Muscular Atrophy. Sanofi Genzyme's option for each program is triggered following the completion of the first proof of principle human clinical study on a program-by-program basis.

Subject to specified exceptions, we are solely responsible for all costs incurred in connection with the development of each of the covered programs prior to Sanofi Genzyme's exercise of its option for such program. Upon Sanofi Genzyme's exercise of its option to license most of the programs pursuant to our collaboration, we will have sole responsibility for the development and commercialization of such product in the United States, and Sanofi Genzyme shall have sole responsibility for development and commercialization of such product in the rest of the world. In the case of our Huntington's disease program, if Sanofi Genzyme exercises its co-commercialization rights, it will also be responsible for commercialization activities related to the Huntington's disease product in the United States. In the case of our Spinal Muscular Atrophy product, if Sanofi Genzyme exercises its option, it will be responsible for all development costs occurring following the option exercise date and all worldwide commercialization activities.

In February 2018, we entered into an agreement in connection with the AbbVie Collaboration, or the AbbVie Collaboration Agreement, pursuant to which we granted AbbVie an exclusive option to license, develop, and commercialize AAV and other virus-based gene therapy products for the treatment of neurodegenerative diseases related to defective or excess aggregation of tau protein in the human brain, including Alzheimer's disease. The collaboration is comprised of a research period, a development period, and an exclusive license option. During the research period, we are obligated to use diligent efforts to conduct antibody engineering and other research activities to create research compounds and to develop product candidates. We will be solely responsible for the costs and expenses during the research period. During a specified portion of the research period, AbbVie may exercise one or more of its exclusive development options to select up to a total of three research compounds and their corresponding product candidates to proceed to the development period.

During the development period, we are obligated to use diligent efforts to conduct development activities, including IND-enabling and Phase 1 clinical trial activities, for such selected research compounds and their corresponding product candidates. We will be solely responsible for the costs and expenses during the development period. During a specified portion of the development period, AbbVie may exercise its exclusive license option to further develop and commercialize all of the research compounds and corresponding product candidates. Upon the exercise of its license option, AbbVie would be solely responsible for all development and commercialization activities relating to the licensed compounds and corresponding licensed products, subject to certain exceptions. We also may elect to share in AbbVie's development costs relating to a licensed product on an indication-by-indication basis in exchange for a specified increase in royalties.

Other than the above, there were no material changes to our contractual obligations and commitments described under Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, as filed with the SEC on March 14, 2018.

Off-Balance Sheet Arrangements

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

JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an emerging growth company, or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies.

Subject to certain conditions, as an EGC, we intend to rely on certain of these exemptions, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.07 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risk related to changes in interest rates. We have policies requiring us to invest in high-quality issuers, limit our exposure to any individual issuer, and ensure adequate liquidity. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash equivalents, are in the form of money market funds and marketable securities and are invested in U.S. Treasury obligations. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We are not currently exposed to market risk related to changes in foreign currency exchange rates; however, we may contract with vendors that are located in Asia and Europe in the future and may be subject to fluctuations in foreign currency rates at that time.

ITEM 4. CONTROLS AND PROCEDURES

Management's Evaluation of Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) or 15d-15(e) under the Exchange Act to mean controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms. Our disclosure controls and procedures include, without limitation, controls and other procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2018. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based

upon the evaluation described above that, as of June 30, 2018, our disclosure controls and procedures were effective at the reasonable assurance level.

We continue to review and document our disclosure controls and procedures and may from time to time make changes aimed at enhancing their effectiveness and to ensure that our systems evolve with our business.

Changes in Internal Control over Financial Reporting

During the three months ended June 30, 2018, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

As of the date of this Quarterly Report on Form 10-Q, we were not party to any material legal matters or claims. In the future, we may become party to legal matters and claims arising in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations, or cash flows.

ITEM 1A. RISK FACTORS

The following risk factors and other information in this Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and related notes thereto, should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Quarterly Report on Form 10-Q for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Capital

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

We are a clinical-stage gene therapy company with a limited operating history and have not yet generated revenues from the sales of our product candidates. Investment in biotechnology companies is highly speculative because it entails substantial upfront capital expenditures and significant risk that the product candidate will fail to obtain regulatory approval or become commercially viable. We have not yet demonstrated the ability to complete any clinical trials of our product candidates, obtain marketing approvals, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful commercialization. We continue to incur significant expenses related to research and development, and other operations in order to commercialize our product candidates. As a result, we are not and have never been profitable and have incurred losses since our inception. Our losses were \$45.5 million and \$35.5 million for the six months ended June 30, 2018 and 2017, respectively. As of June 30, 2018, we had an accumulated deficit of \$226.2 million.

We historically have financed our operations primarily through private placements of our redeemable convertible preferred stock, public offerings of our common stock, and our collaboration with Sanofi Genzyme, which we refer to as the Sanofi Genzyme Collaboration, and our collaboration with AbbVie Biotechnology Ltd., or AbbVie, which we refer to as the AbbVie Collaboration. On November 16, 2015 we closed our initial public offering whereby we sold 5,750,000 shares of common stock at a public offering price of \$14.00 per share, including 750,000 shares of common stock issued upon the full exercise by the underwriters of their option to purchase additional shares, resulting in net proceeds to us of \$72.9 million after deducting underwriting discounts and commissions and offering expenses

payable by us. On November 7, 2017, we sold 5,175,000 shares of common stock to the public at an offering price of \$12.00 per share, including 675,000 shares of common stock issued upon the full exercise by the underwriters of their option to purchase additional shares, resulting in net proceeds to us of \$58.0 million after deducting underwriting discounts, commissions, and offering expenses payable by us. To date, we have devoted substantially all of our financial resources to building our gene therapy platform, selecting product programs, conducting research and development, including preclinical development of our product candidates, building our intellectual property portfolio, building our team, and establishing the Sanofi Genzyme Collaboration and the AbbVie Collaboration. We expect that it could be several years, if ever, before we have a commercialized product candidate. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if, and as, we:

- continue investing in our gene therapy platform to optimize vector engineering, manufacturing and dosing and delivery techniques;
- continue to advance our clinical candidate, VY-AADC, through the ongoing Phase 1b clinical trial and into a pivotal Phase 2-3 clinical program as a treatment for Parkinson's disease;
- initiate additional preclinical studies and clinical trials for, and continue research and development of, our other programs;
- conduct joint research and development under the AbbVie Collaboration for the research, development, and commercialization of adeno-associated virus, or AAV, and other virus-based gene therapy products for the treatment of diseases of the central nervous system and other neurodegenerative diseases related to defective or excess aggregation of tau protein in the human brain, including Alzheimer's disease;
- continue our process research and development activities, as well as establish our research-grade and commercial manufacturing capabilities;
- identify additional neurological diseases for treatment with our AAV gene therapies and develop additional programs or product candidates;
- work to identify and optimize novel AAV capsids;
- develop, obtain and maintain regulatory clearances for devices to deliver our AAV gene therapies;
- seek marketing and regulatory approvals for VY-AADC or other product candidates or devices that arise from our programs that successfully complete clinical development;
- maintain, expand and protect our intellectual property portfolio;
- identify, acquire or in-license other product candidates and technologies;
- develop a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- expand our operational, financial and management systems and personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- increase our product liability and clinical trial insurance coverage as we expand our clinical trials and commercialization efforts; and

- continue to operate as a public company.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses will increase if:

- we are required by the U.S. Food and Drug Administration, or FDA, or the European Medicines Agency, or EMA, or other regulatory agencies to perform trials or studies in addition to those currently expected;
- there are any delays in receipt of regulatory clearance to begin our planned clinical programs or to use companion devices required in such clinical programs; or
- there are any delays in enrollment of patients in or completing our clinical trials or the development of our product candidates.

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 clinical trials of our product candidates; obtaining marketing approval for these product candidates; developing and obtaining marketing approval of any required companion devices; manufacturing at clinical and commercial scale; marketing and selling those products that are approved; satisfying any post-marketing requirements and achieving an adequate level of market acceptance of and obtaining and maintaining adequate coverage and reimbursement from third-party payors for such products; and protecting our rights to our intellectual property portfolio. 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 our stockholders to lose all or part of their investment.

We may not be able to generate sufficient revenue from the commercialization of our product candidates and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with our collaborative partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our current and future product candidates. Our lead product candidate VY-AADC is being evaluated in a Phase 1b clinical trial and is advancing into a pivotal Phase 2-3 clinical trial in 2018, and we do not anticipate generating revenues from product sales for the next several years, and we may never succeed in doing so. Our ability to generate future revenues from product sales depends heavily on our and our collaborators' success in:

- completing preclinical and clinical development of our product candidates and any required companion devices and identifying new product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval by establishing a sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- obtaining and maintaining adequate coverage and reimbursement by government and third-party payors for our product candidates if and when approved;

- maintaining and enhancing a sustainable, scalable, reproducible and transferable manufacturing process for our vectors and product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for our product candidates, if and when approved;
- obtaining an adequate level of market acceptance of our product candidates as a viable treatment option;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- obtaining, maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding and defending against third-party claims of interference or infringement; and
- attracting, hiring and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, EMA, or other regulatory authorities to perform preclinical studies and clinical trials in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will need to raise additional funding, which 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 certain of our product development efforts or other operations.

We expect our expenses to increase in connection with our ongoing and planned activities, particularly as we continue the research and development of, continue or initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant expenses related to product sales, medical affairs, marketing, manufacturing and distribution. Since the completion of our IPO on November 16, 2015, we have also incurred costs associated with 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 or enter into business development transactions when needed or on acceptable terms, we could be forced to delay, reduce or eliminate certain of our research and development programs or any future commercialization efforts.

Our operations have consumed significant amounts of cash since inception. As of June 30, 2018, our cash, cash equivalents, and marketable debt securities were \$197.0 million. Based upon our current operating plan, we expect that our existing cash, cash equivalents, and marketable debt securities, will enable us to fund our operating expenses and capital expenditure requirements into early 2020.

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

- the scope, progress, results, and costs of product discovery, preclinical studies and clinical trials for our product candidates and any required companion devices;
- the scope, progress, results, costs, prioritization, and number of our research and development programs;
- the progress and status of the Sanofi Genzyme Collaboration and the AbbVie Collaboration, including any research and development costs for which we are responsible, the potential exercise by our collaboration partners of options to develop or license certain products and product candidates, and our potential receipt of future milestone payments and royalties from our collaboration partners;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, preclinical development and clinical trial costs, or the achievement of milestones or occurrence of other developments that trigger payments, under any other collaboration agreement to which we might become a party;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaboration, distribution, or other marketing arrangements for our product candidates on favorable terms, if at all;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies or acquire or invest in other businesses, such as our investment in MRI Interventions, Inc., or MRIC;
- the costs related to evaluating possible alternative devices that may be useful in the delivery of our product candidates, including our ongoing development of the trajectory array guide device;
- the costs of securing manufacturing arrangements for pre-commercial and commercial production;
- the level of product sales from any product candidates for which we obtain marketing approval in the future; and
- the costs of establishing or contracting for sales, manufacturing, marketing, distribution, and other commercialization capabilities if we obtain regulatory approvals to market our product candidates.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive, and uncertain process that takes years to complete. We may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenues, if any, and any commercial milestones or royalty payments under our collaboration agreements, will be derived from sales of products that may not be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing and business development to achieve our business objectives. Adequate additional financing or business development transactions may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate product revenues sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. We do not have any committed external source of funds other than the amounts we are entitled to receive from our collaboration partners for potential option exercises, the achievement of specified regulatory and commercial milestones, and royalty payments under our collaboration agreements. To the extent that we raise additional capital through the sale of equity or equity-linked securities, including convertible debt, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our existing stockholders' rights as holders of our common stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, obtaining additional capital, acquiring or divesting businesses, making capital expenditures or declaring dividends. Our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our common stock to decline. Further, our existing stockholders may not agree with the terms of such financings.

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

Our limited operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability.

We are an early-stage company. Our operations to date have been limited to building our team, business planning, raising capital, establishing our intellectual property portfolio, determining which neurological diseases to pursue, advancing our product candidates including delivery and manufacturing and conducting preclinical studies and clinical trials. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. To achieve our current goals, we will need to transition in the future from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Risks Related to the Development and Regulatory Approval of Our Product Candidates

Our AAV gene therapy product candidates are based on a relatively novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all. Only three gene therapy products have been approved in the United States and only two such products have been approved in the European Union.

We have concentrated our research and development efforts to date on our gene therapy platform, identifying our initial targeted disease indications, and our initial product candidates. Our future success depends on our successful development of viable AAV gene therapy product candidates. Currently, only one of our product candidates, VY-

AADC, is in clinical development, and the remainder of our product candidates are in preclinical development. We cannot accurately predict when or if any of our product candidates will prove effective or safe in humans or whether these product candidates will receive marketing approval. There can be no assurance that we will not experience problems or delays in developing our product candidates and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved. We also may experience unanticipated problems or delays in expanding our manufacturing capacity.

The clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. The regulatory approval process for novel product candidates such as gene therapies can be more expensive and take longer than for other, better known or more extensively studied product candidates. Until August 2017, the FDA had never approved a gene therapy product. Since that time, it has approved Kymriah by Novartis International AG, for pediatric and young adult patients with a form of acute lymphoblastic leukemia, Yescarta by Kite Pharma, Inc., for adult patients with certain forms of non-Hodgkin lymphoma, and Luxturna by Spark Therapeutics, Inc., or Spark, for patients with an inherited form of vision loss. Similarly, only two gene therapy products, Glybera by uniQure N.V., or uniQure, which has since been withdrawn from the market by uniQure, and Strimvelis by GlaxoSmithKline PLC, have received marketing authorization from the European Commission.

It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or the European Union or how long it will take to commercialize our product candidates. The few regulatory approvals to date may not be indicative of what the FDA, European Commission, or other regulatory authorities may require for approval or whether different or additional preclinical studies or clinical trials may be required to support regulatory approval in a particular jurisdiction. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects may be harmed.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. Such requirements may lengthen the regulatory requirements review process, require us to perform additional studies, and increase our development costs or may force us to delay, limit, or terminate certain of our programs.

The Center for Biologics Evaluation and Research, or CBER, of the FDA regulates biological products for human use. The Office of Tissues and Advanced Therapies, or OTAT, formerly known as the Office of Cellular, Tissue and Gene Therapies, within CBER reviews gene therapy and related products and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER in its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the National Institutes of Health, or NIH, are also potentially subject to review by the NIH's Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RAC. Even though the FDA decides whether individual gene therapy protocols may proceed, the RAC public review process, if undertaken, can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and permitted its initiation. Conversely, the FDA may place an Investigational New Drug application, or IND, on a clinical hold even if the RAC has provided a favorable review or an exemption from in depth, public review.

NIH-funded institutions need to have their institutional biosafety committee, or IBC, as well as their institutional review board, or IRB, review proposed clinical trials to assess the safety of the trial. The Phase 1b clinical trial of VY-AADC and the separate Phase 1 trial exploring the delivery of VY-AADC using a posterior trajectory are being conducted at the University of California San Francisco, or UCSF, and University of Pittsburgh Medical Center, or UPMC, and two other sites and therefore are subject to oversight by these authorities. Such trials will need to be re-reviewed by the respective institutional IRBs if the protocol for the trial is further amended. For any new clinical trial protocols, including those of our randomized, placebo-controlled Phase 2 trial and our planned randomized, placebo-controlled Phase 3 trial, the same processes and issues apply.

Adverse developments in clinical trials of gene therapy products conducted by us or others may cause the FDA or other oversight bodies to change the requirements for approval of any of our product candidates. Similarly, EMA and local health authorities of individual countries within the European Union may issue new guidelines concerning the clinical development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. The EMA and agencies at both the federal and state level in the United States have expressed an interest in further regulating new biotechnologies, including gene therapy. In addition, gene therapy products are considered genetically-modified organism, or GMO, products and are regulated as such in each country. Designation of the type of GMO product and subsequent handling and disposal requirements can vary across countries and is variable throughout the EU. Addressing each specific country requirement and obtaining approval to commence a clinical trial in these countries could result in delays in starting, conducting, or completing a clinical trial. Similar issues could be faced in other regions of the world including the Asia-Pacific region.

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, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. For example, we recently sought guidance from the FDA through a Type C meeting regarding, among other matters, the regulatory pathway for VY-AADC. In advance of the proposed meeting, we received preliminary written responses to questions we had previously submitted; we believe such responses were complete and, as a result, decided that a meeting was unnecessary. If we fail to consult or solicit guidance from regulators, we may be required to delay or discontinue development of certain of our 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 increased or lengthier regulatory approval process and further restrictions on development of our product candidates can be costly and could negatively impact our or our collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

Results from preclinical studies and early-stage clinical trials may not be indicative of efficacy in late-stage clinical trials.

All of our product candidates are in early stages of development. Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later stage clinical trials, interim results of a clinical trial do not necessarily predict final results and results from one completed clinical trial may not be replicated in a subsequent clinical trial with a similar study design. Some of our clinical trials, including our Phase 1 clinical trials and our Phase 1b clinical trial for VY-AADC, were conducted with small patient populations and were not blinded or placebo-controlled, making it difficult to predict whether the favorable results that we observed in such trials will be repeated in larger and more advanced clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage clinical trials. If a larger population of patients does not experience positive results, if these results are not reproducible, or if our products show diminishing activity over time, our products may not receive approval from the EMA or the FDA. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may encounter regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of product development. Failure to confirm favorable results from earlier trials by demonstrating the safety and effectiveness of our products in late-stage clinical trials with larger patient populations could harm our business and we may never succeed in commercialization or generating product revenue.

The doses and coverage of the putamen being employed in the ongoing VY-AADC Phase 1b clinical trial are higher than those used in prior trials and may need to be further optimized or we may not generate sufficient clinical data in a placebo-controlled trial to achieve market authorization. Further, any favorable results which we obtain from our Phase 1b clinical trial might not be replicated in subsequent trials.

The clinical trial results of some of our collaborators have been negatively affected by factors that had not been fully anticipated prior to the examination of the trial results. For example, the magnitude of some of the clinical responses seen in the Phase 1 clinical trial of AAV2-AADC conducted by UCSF were similar to placebo effects observed in previous surgical therapies for Parkinson's disease. As a result, we are unable to rely on the results of this Phase 1 trial for an indication of the efficacy of treatment with VY-AADC. We believe that there is a need to optimize the dose and volume of infusion of VY-AADC to substantially increase the coverage of the putamen, the region of the brain targeted by VY-AADC, to achieve a clinical benefit. However, we can provide no assurances that we will be able to optimize these parameters and thereby achieve sufficient coverage of the putamen to achieve a clinical benefit.

The ongoing Phase 1b clinical trial of VY-AADC incorporates several design features in an attempt to increase the area of the putamen, particularly the posterior putamen, which receives VY-AADC treatment. We are employing larger infusion volumes and higher doses of VY-AADC, and we are using the ClearPoint® System to provide real-time, intra-operative, magnetic resonance imaging, or MRI, assistance to the physician surgically administering VY-AADC to the patient.

In a separate Phase 1 clinical trial, we are also exploring a posterior, or back of the head, delivery approach of drug into the putamen, compared to a transfrontal, or top of the head, delivery approach used in Cohorts 1 through 3 of the ongoing Phase 1b clinical trial described above. A posterior approach better aligns the infusion of VY-AADC with the anatomical structure of the putamen to potentially reduce the total procedure time and increase the total coverage of the putamen. Administration of VY-AADC with this posterior approach has been well-tolerated with no reported SAEs, with most patients discharged from the hospital the day after surgery.

Due to the nature of the techniques being used in the Phase 1b clinical trial and the numerous variables that can be changed, it is possible that the data generated from this trial may not provide evidence of clinical benefit. For example, physicians may use cannulas, which are small tubes, of differing lengths in the infusion procedure, or may use differing infusion speeds or infusion angles. These differences could affect the dose of VY-AADC that ultimately reaches the putamen, leading to highly variable results. Similarly, we have limited experience to date with the posterior delivery approach we intend to use in the Phase 2-3 clinical program, and it may not generate outcomes that are clinically superior to those of the transfrontal approach.

Informed by the results of the Phase 1 clinical trials, we have determined that the posterior approach is the preferred surgical route of administration for the pivotal Phase 2-3 clinical program. For the pivotal Phase 2 trial, we have selected a dose of up to 2.5×10^{12} vector genomes, which is defined as a maximum total bilateral dose. This dose is between the up to maximum total vector genome doses administered in Cohorts 2 and 3 from the Phase 1b trial when considering the higher volume administered with the posterior trajectory and vector produced using the baculovirus system. We have not previously evaluated this dose in a clinical trial. The dose concentration and volume we have selected for the pivotal program may not achieve the desired safety and efficacy in the Phase 2 and planned Phase 3 randomized, controlled clinical trials.

The Phase 2 trial is a randomized, placebo-controlled trial with a planned enrollment of up to 42 patients who have been diagnosed with Parkinson's disease for at least four years. Patients will be randomized 1:1 to either VY-AADC or placebo surgery. After treatment with either VY-AADC or placebo surgery, patients will be followed in a blinded manner for 12 months, at which point, the trial will unblind, and safety and efficacy measures will be assessed. The primary efficacy endpoint of the trial is the improvement from baseline to 12 months in a patient's self-reported diary on-time without troublesome dyskinesia in the VY-AADC treatment arm compared to the placebo surgery arm. Multiple secondary endpoints include the assessment of other motor function from patient diaries as well as assessments from the Unified Parkinson's Disease Rating Scale (UPDRS) scores, including UPDRS-3 and UPDRS-2 scores. The Phase 2 trial is 80% powered to detect a 2.0 hour improvement in the primary endpoint of diary on-time without troublesome dyskinesia from baseline to twelve months for the treatment arm compared with the placebo arm.

We are using a different manufacturing process for our AAV gene therapy vector in later stage Parkinson's clinical trials. We have begun to manufacture VY-AADC using our baculovirus/Sf9 system as opposed to manufacturing in HEK 293 cells, which were used in our Phase 1 clinical trials. We have conducted studies to demonstrate comparability between the current version and the new version. It is possible, however, that the results of our pivotal Phase 2-3 clinical program in Parkinson's disease may differ from the results of our Phase 1b or our Phase 1 posterior clinical trials based on VY-AADC manufactured using our baculovirus/Sf9 system.

We intend to conduct, and may in the future conduct, clinical trials for product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.

To date, we have only conducted clinical trials in the United States. However, we may in the future choose to conduct, one or more of our clinical trials or include sites in current or future clinical trials outside the United States. We generally plan to conduct our later stage and pivotal clinical trials of our product candidates globally.

Although the FDA may accept data from sites or clinical trials outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials or trial sites are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials or trial sites also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial or trial site outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and would delay or permanently halt our development of the applicable product candidates.

Other risks inherent in conducting international clinical trials or using international trial sites include:

- foreign regulatory requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment;
- failure of enrolled patients to adhere to clinical protocols or inadequate collection and assessment of clinical data as a result of differences in healthcare services or cultural customs;
- foreign exchange fluctuations;
- diminished or loss of protection of intellectual property in the relevant jurisdiction; and
- political and economic risks relevant to foreign countries.

We may encounter substantial delays or difficulties in commencement, enrollment or completion of our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, which could prevent us from commercializing our current and future product candidates on a timely basis, if at all.

Before obtaining marketing approval from regulatory authorities for the sale of our current and future product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates. Clinical trials are expensive, time-consuming and their outcomes are uncertain.

We have very limited experience with clinical trials. The ongoing Phase 1b clinical trial of VY-AADC and the separate Phase 1 trial exploring the delivery of VY-AADC using a posterior trajectory are being conducted at four locations including UCSF and UPMC. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A clinical trial failure can occur at any stage of testing. Similarly, there may be delays or difficulties in our initiation of future clinical trials. Due to the additional regulatory uncertainties associated with gene

therapy products, we did not initiate our pivotal Phase 2-3 clinical trial for our clinical candidate, VY-AADC, as a treatment for Parkinson's disease until we met with OTAT to discuss our proposed trial design and overall development plan. While we have received OTAT's feedback, and incorporated it as appropriate in our plans, the clinical trials as designed may not achieve the prospectively defined primary clinical endpoints or provide a favorable benefit to risk ratio to support a biologics license application, or BLA, filing or approval.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner or at all pursuant to the requirements of the FDA, EMA, or other regulatory authorities. Patient enrollment and trial completion are affected by many factors including:

- perceived risks and benefits of AAV gene therapy approaches for the treatment of neurological diseases;
- perceived risks of the delivery procedure, such as intracranial infusion for VY-AADC;
- formulation changes to our product candidates may require us to conduct additional clinical studies to bridge our modified product candidates to earlier versions;
- size of the patient population and process for identifying patients;
- design of the trial protocol;
- eligibility and exclusion criteria;
- patients with preexisting antibodies to the vector gene therapy vector that preclude their participation in the trial;
- perceived risks and benefits of the product candidate under study;
- availability of competing therapies and clinical trials;
- severity of the disease under investigation;
- availability of genetic testing for potential patients;
- proximity and availability of clinical trial sites for prospective patients;
- lack of adequate compensation of patients;
- ability to obtain and maintain patient consent;
- risk that enrolled patients will drop out before completion of the trial;
- our ability to locate appropriately trained physicians to conduct such clinical trials, which may be particularly difficult for the VY-AADC clinical trial, in which we are currently using the ClearPoint System, which is only available at a small number of academic medical centers in the United States;
- our ability to develop and obtain regulatory approval of the trajectory array guide device, our real-time, intra-operative, MRI-compatible device, and to train physicians to conduct clinical trials using the device;

- willingness of patients to participate in a placebo-controlled trial;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

Further, we plan to seek marketing approvals in the United States, the European Union and other jurisdictions, which may require that we conduct clinical trials in foreign countries. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with clinical research organizations, or CROs, and physicians;
- different standards for the conduct of clinical trials;
- absence in some countries of established groups with sufficient regulatory expertise for review of AAV gene therapy protocols;
- our inability to locate qualified local partners or collaborators for such clinical trials; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would harm our business, financial condition, results of operations and prospects.

Other events that may prevent successful or timely completion of clinical development include:

- delays in reaching a consensus with regulatory authorities on trial design;
- delays in initiating trials due to any additional review that is required by RAC;
- delays in reaching agreement on acceptable terms with prospective CROs, and clinical trial sites;
- delays in opening clinical trial sites or obtaining required IRB or independent ethics committee approval at each clinical trial site;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites; or our decision or the requirement of regulators or institutional review boards to suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- failure by us, any CROs we engage, or any other third parties to adhere to clinical trial requirements or regulatory requirements;
- failure by us, any CROs we engage, or any other third parties to perform in accordance with the FDA's good clinical practices, or GCP, or applicable regulatory guidelines in the European Union;

- failure by physicians to adhere to delivery protocols leading to variable results;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions;
- insufficient or inadequate supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates, including potential delays in our pivotal Phase 2-3 clinical trial in Parkinson's disease associated with the development of the trajectory array guide device;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites or patients dropping out of a trial at a rate higher than we anticipate;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- receipt of negative or inconclusive clinical trial results;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; or
- the cost of clinical trials of our product candidates may be greater than we anticipate.

Any inability to successfully complete preclinical studies and clinical trials could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;

- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a Risk Evaluation and Mitigation Strategy, or REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Our product candidates or the process for administering our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.

In past clinical trials that were conducted by others with non-AAV gene therapy vectors, several significant side effects were caused by gene therapy treatments, including reported cases of leukemia and death. Other potential side effects could include an immunologic reaction and insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation. If our vectors demonstrate a similar adverse effect, or other adverse effects, we may be required to halt or delay further clinical development of our product candidates or withdraw the product from the market post-approval. For example, in a recently published review of patients with hepatocellular carcinomas, it was shown that a small subset contained an integrated genome sequence of wild-type AAV2 and it was suggested that AAV2 may be associated with insertional oncogenesis.

In addition to side effects caused by the product candidate, the administration process or related procedures also can cause side effects. VY-AADC and VY-HTT01 will be administered directly to the targeted areas and cells in the brain, requiring the patient to undergo brain surgery. In a previous Phase 1 clinical trial conducted by UCSF, three patients experienced hemorrhages caused by the surgical procedure for administering VY-AADC. In the ongoing Phase 1b clinical trial of VY-AADC, we are using the ClearPoint System, which has only been used in limited gene therapy neurosurgeries to date to provide accurate placement of the cannula in the putamen, to allow for real-time, intra-operative MRI to assist the physician in visualizing the delivery of VY-AADC to the putamen and to avoid specific blood vessels during the duration of the surgical procedure, with the goal of reducing the risk of hemorrhages. One patient in the ongoing Phase 1b trial at UCSF experienced two serious adverse events, or SAEs, a pulmonary embolism, or blood clot in the lungs, and related heart arrhythmia, or irregular heartbeat, which were determined to be related to the surgical procedure and prolonged immobility, not VY-AADC. In future trials, we may use the trajectory array guide device, a proprietary real-time, intra-operative, MRI-compatible device that we are currently developing. If other side effects were to occur in connection with the surgical procedure, or problems were encountered with the use of our trajectory array guide device, our clinical trials could be suspended or terminated.

If in the future we are unable to demonstrate that such side effects were caused by the administration process or related procedures or are unable to modify the trial protocol adequately to address such side effects, 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. For products that “knock down” or reduce the amount of a gene or its encoded protein, their effects on other parts of the body, or “off target” effects, could result in unforeseen toxicity. Even if we are able to demonstrate that any future SAEs are not product-related, and regulatory authorities do not order us to cease further development of our product candidates, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any 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 outweigh its risks. Such REMS 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 or the limitation of the use of the product to specifically trained neurosurgeons and/or certain centers. Furthermore, adverse events which were initially considered unrelated to the study treatment of the clinical trial may later be found to be caused by the study treatment. If we or others later identify undesirable side effects caused by our product candidate, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate 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 events could prevent us from achieving or maintaining market acceptance of our product candidates and could significantly harm our business, prospects, financial condition and results of operations.

We may be unable to obtain orphan drug designation or exclusivity for any of our product candidates for which we seek such designation. If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug 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.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, or the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug or biological product if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug or biological product will be recovered from sales in the United States. We have received feedback from the FDA that VY-AADC for the treatment of Parkinson's disease does not qualify for orphan disease designation because the potential for its use in earlier stages of Parkinson's disease exceeds the 200,000 patient population criteria in the United States. In the European Union, EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product. We have received feedback from the Committee for Orphan Medicinal Products that orphan designation likely would not be granted for VY-AADC in Parkinson's disease since the Committee does not grant such status for products targeting more severe stages of a disease.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the European Commission from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we may be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the European Union. The exclusivity period in the United States can be extended by nine months if the BLA sponsor submits pediatric data that adequately respond to a written request from the FDA for such data. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer

justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

We believe that all of our current programs may qualify for orphan drug designation except for VY-AADC for Parkinson's disease. Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs or biological products can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug or biological product for the same condition if the FDA concludes that the latter drug or biological product is not the same drug or biological product or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the European Union, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

Even if we seek orphan drug designation from the FDA, the European Commission or other regulatory agencies for a product candidate, there can be no assurances that the regulatory agency or agencies will grant such designation. Additionally, the designation of any of our product candidates as an orphan drug does not guarantee that any regulatory agency will ultimately approve that product candidate.

On August 3, 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

A potential breakthrough therapy designation by the FDA for 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.

We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug or biological product that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biological product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs or biological products that have been designated as breakthrough therapies, 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. Drugs designated as breakthrough therapies by the FDA may also be eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead

determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the drugs or biological products no longer meet the conditions for qualification.

A potential regenerative medicine advanced therapy designation by the FDA for 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.

We may seek a regenerative medicine advanced therapy, or RMAT, designation for some of our product candidates. Under the 21st Century CURES Act, or the CURES Act, to be eligible to receive RMAT designation from the FDA, a product candidate must be (i) considered a “regenerative medicine therapy” as defined in the Cures Act; (ii) intended to treat, modify, reverse, or cure one or more serious or life-threatening diseases or conditions; and (iii) indicated, in preliminary clinical evidence, to have the potential to address unmet medical needs for such diseases or conditions. Gene therapies, including genetically modified cells, that lead to a durable modification of cells or tissues may meet the definition in the Cures Act of a regenerative medicine therapy.

The RMAT program is intended to facilitate efficient development and expedite review of such therapies. A new drug application or a BLA for a product candidate that has received an RMAT designation may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A product candidate that has received an RMAT designation that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval.

In June 2018, the FDA granted RMAT designation for our VY-AADC gene therapy treatment for Parkinson’s disease in patients with motor fluctuations that are refractory to medical management. The designation was based on data from our Phase 1b clinical trial.

RMAT designation is within the discretion of the FDA. Accordingly, even if we believe one of our other 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 conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, the FDA may later decide that product candidate that received RMAT designation no longer meets the conditions for designation.

Fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process and does not assure FDA approval of our product candidate.

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical need for this condition, the drug sponsor may apply for FDA fast track designation. VY-AADC has been granted fast track designation by the FDA. We may seek such a designation for our other product candidates. A fast track designation does not ensure that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. Thus, fast track products may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA’s priority review procedures.

Priority review designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval of our product candidate.

If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the FDA's goal to review an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or any future collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize our products, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and comparable regulatory authorities in other countries. 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 only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. 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.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive; may take many years if additional clinical trials are required, 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. In the United States, for example, the submission fee to obtain U.S. marketing approval is more than \$2.0 million, and may be higher in the future. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries 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, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Accordingly, if we or any future collaborators experience delays in obtaining approval or if we or they fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory oversight.

Even if we obtain any regulatory approval for our product candidates, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storing, advertising, promoting, sampling, record-keeping and submitting safety and other post-market information. Any regulatory approvals that we receive for our product candidates also may be subject to a REMS, limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the quality, safety and efficacy of the product. For example, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years. The holder of an approved BLA also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP, requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory authority may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory authority may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application, or any supplements thereto, submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the product;
- seize or detain the product or otherwise require the withdrawal of the product from the market;
- refuse to permit the import or export of products; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and adversely affect our business, financial condition, results of operations and prospects.

In addition, FDA policies, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would harm our business, financial condition, results of operations and prospects.

We face significant competition in an environment of rapid technological change and the possibility 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, intense and dynamic competition to develop new technologies and proprietary therapies, and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

We are aware of several companies focused on developing gene therapies in various indications, including bluebird bio, Inc., Abeona Therapeutics, Inc., Adverum Biotechnologies, Inc., Aevitas Therapeutics, Inc., Actus Therapeutics, Inc., Agilis Biotherapeutics, LLC (acquired by PTC Therapeutics, Inc. in July 2018), or Agilis, Applied Genetic Technologies Corporation, Alector, Asklepios BioPharmaceutical, Inc., Audentes Therapeutics, Inc., AveXis, Inc. (acquired by Novartis in April, 2018), Axovant Sciences, Ltd., GenSight Biologics SA, LogicBio Therapeutics, Inc., Lysogene SA, MeiraGTx Ltd., NightstaRx Ltd, Prevail Therapeutics, Inc., REGENXBio Inc., Solid Biosciences, Inc., uniQure NV, Pfizer, Inc., or Pfizer, and Spark, as well as several companies addressing other methods for modifying genes and regulating gene expression. Any advances in gene therapy technology made by a competitor may be used to develop therapies that could compete against any of our product candidates.

We expect that VY-AADC will compete with a variety of therapies currently marketed and in development for Parkinson's disease, including deep brain stimulation, or DBS, a device-based treatment for Parkinson's disease marketed by Medtronic plc, Abbott Laboratories (acquired from St. Jude Medical in 2017), and other medical device companies; DUOPA/Duodopa marketed by AbbVie Inc.; and other novel, non-oral forms of levodopa in development, including NeuroDerm's ND0612 (acquired by Mitsubishi Tanabe Pharma in 2017), Acorda Therapeutics' inhaled levodopa, CVT-301, and Sunovion Pharmaceuticals' sublingual apomorphine, APL-130277 (acquired from Cynapsus Therapeutics). Gene therapy competition for Parkinson's disease previously included AMT-090 or AAV-GDNF, but this was deprioritized by uniQure in 2016. Axovant Sciences, Ltd. purchased the rights to Oxford Biomedica plc's product and is planning for a Phase 1/2 trial in 2018 for a second generation LentiVector gene therapy.

We expect that our preclinical programs will compete with a variety of therapies in development, including:

- VY-SOD101 for a monogenic form of ALS will potentially compete with IONIS-SOD1Rx being developed by Ionis Pharmaceuticals, Inc., or Ionis, in collaboration with Biogen Inc., or Biogen, and a gene therapy being developed by AveXis;
- VY-FXN01 for Friedreich's ataxia will potentially compete with AAV-FXN being developed by Adverum Biotechnologies, AAV-FXN being developed by Pfizer, and frataxin targeted gene therapy being developed by Agilis, and BMN 290 being developed by BioMarin Pharmaceutical Inc.;
- VY-HTT01 for Huntington's disease will potentially compete with IONIS-HTTRx being developed by Ionis in collaboration with F. Hoffmann-La Roche Ltd., or Roche, WVE-120101 and WVE-120102 being developed by WAVE Life Sciences in collaboration with Takeda Pharmaceuticals, a Zinc Finger Protein (ZFP) therapy being developed by Sangamo Therapeutics, Inc. in collaboration with Shire plc (acquired by Takeda in May, 2018), and gene therapies being developed by uniQure and Spark;

- Our tau-related diseases program for tauopathies including Alzheimer's disease, PSP, and FTD will potentially compete with tau antibodies being developed by Genentech Inc. (wholly owned subsidiary of Roch Holding AG) in collaboration with AC Immune SA, Eli Lilly & Co., AbbVie Inc., Biogen, and several other companies, as well as an antisense oligonucleotide program being developed by Ionis in collaboration with Biogen; and
- VY-NAV01 for severe, chronic pain will potentially compete with Na_v1.7 inhibitors being developed by Teva Pharmaceuticals, Biogen, Genentech Inc. (wholly owned subsidiary of Roch Holding AG) in collaboration with Xenon Pharmaceuticals, Inc., Amgen, Inc., and Astellas Pharma Inc, and Na_v1.8 inhibitors being developed by Vertex.

We are also aware of several companies and institutions who have developed or are developing real-time, intra-operative, MRI-compatible devices that would compete with the trajectory array guide device. Investigators in the Phase 1b clinical trial of VY-AADC and the separate Phase 1 posterior trajectory trial have used the ClearPoint System from MRIC.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources, 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. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative agreements with large and established companies. 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 products that we may develop. Competitors also may obtain FDA or other regulatory approval for their products more rapidly or earlier than us or may obtain orphan drug or other marketing exclusivity, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed or acquired by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors. These third parties also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites, and registering patients for clinical trials.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and operations will be harmed.

Even if we obtain and maintain approval for our product candidates from the FDA, we may never obtain approval for our product candidates outside of the United States, which would limit our market opportunities and adversely affect our business.

Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries also must approve the manufacturing and marketing of the product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. We intend to submit a marketing authorization application to EMA for approval of our product candidates in the European Union but obtaining such approval from the European Commission following the opinion of EMA is a lengthy and expensive process. Even if a product candidate is approved, the FDA or the European

Commission may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and the European Union also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for any of our product candidates may be withdrawn. If we fail to comply with the regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects will be harmed.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

Risks Related to Third Parties

To date, all of our revenue has been derived from our collaborations with Sanofi Genzyme and AbbVie, and if either of these collaboration agreements were to be terminated, our business financial condition, results of operations and prospects would be harmed.

In February 2015, we entered into the Sanofi Genzyme Collaboration Agreement to leverage our combined expertise and assets in gene therapy for neurological diseases. Under the Sanofi Genzyme Collaboration Agreement, we received an upfront commitment of approximately \$100.0 million. Pursuant to the agreement, we granted Sanofi Genzyme an exclusive option to license, develop and commercialize (i) ex-U.S. rights to our Parkinson's disease, Friedreich's ataxia and Huntington's disease programs and a future program, or the Split Territory Programs, with an incremental option to co-commercialize the product candidate from our Huntington's disease program in the United States and (ii) worldwide rights to our spinal muscular atrophy program. If Sanofi Genzyme exercises an option for a Split Territory Program, except for our Parkinson's disease program, it is required to make an option exercise payment to us. Furthermore, at the inception of the agreement, we were eligible to receive up to \$745.0 million in the aggregate upon the achievement of specified regulatory and commercial milestones, including tiered royalty payments based on a percentage of net sales of product candidates from the programs for which Sanofi Genzyme exercised its option, or the Optioned Programs. Our research and development activities in connection with the collaboration might not be successful. We cannot accurately predict when or if any of our product candidates will prove effective or safe in humans or whether these product candidates will receive marketing approval. There can be no assurance that we will not experience problems or delays in developing our product candidates and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved. If Sanofi Genzyme were to elect not to exercise an option, we would have incurred significant development expenses but not receive the option exercise payment or be eligible to receive future milestone or royalty payments related to such program. For example, in October 2017, Sanofi Genzyme notified us that it had decided not to exercise its option for the ex-U.S. rights to VY-AADC and terminated the portion of its collaboration with us concerning Parkinson's disease. As a result of Sanofi Genzyme's decision, the Company is no longer entitled to receive up to \$105.0 million of milestone payments related to the Parkinson's program.

If Sanofi Genzyme exercised one or more options, following such exercise, Sanofi Genzyme will have sole responsibility for the development and commercialization of the product candidates from such program in the applicable territory. Sanofi Genzyme will have the sole discretion to determine and direct its efforts and resources, including the

ability to discontinue all efforts and resources it applies to the development and, if approval is obtained, commercialization and marketing of the product candidates covered by the Optioned Programs in the applicable territories. Sanofi Genzyme may not be effective in obtaining approvals for the product candidates developed from the Optioned Programs or in marketing, or arranging for necessary supply, manufacturing or distribution relationships for, any approved products. Furthermore, Sanofi Genzyme may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us. Sanofi Genzyme has a variety of marketed products and product candidates under collaboration with other companies, including some of our competitors, and its own corporate objectives may not be consistent with our best interests. If Sanofi Genzyme fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate from the Optioned Programs in the applicable territories, or if Sanofi Genzyme terminates our collaboration, our business, financial condition, results of operations and prospects would be harmed.

In addition, any dispute or litigation proceedings we may have with Sanofi Genzyme in the future could delay development programs, create uncertainty as to ownership of or access to intellectual property rights, distract management from other business activities and generate substantial expense. Finally, we also may not be able to seek and obtain a viable, alternative collaborator to partner with for the development and commercialization of the Split Territory Programs or the Optioned Programs.

In February 2018, we entered into an exclusive collaboration and option agreement with AbbVie, which we refer to as the AbbVie Collaboration Agreement, for the research, development, and commercialization of AAV gene therapy products for the treatment of diseases of the central nervous system and other neurodegenerative diseases related to defective or excess aggregation of tau protein in the human brain, including Alzheimer's disease. Under the terms of the AbbVie Collaboration Agreement, we received an upfront payment of \$69.0 million and may receive option exercise payments, future development and regulatory milestone payments and royalties.

Under the AbbVie Collaboration Agreement, we are obligated to use diligent efforts to conduct research and development activities, including IND-enabling and Phase 1 clinical trial activities, for which we are solely financially responsible. As described above, our research and development activities in connection with a collaboration might not be successful. The AbbVie Collaboration Agreement shall automatically terminate if AbbVie decides not to exercise one or more of its options prior to the expiration of the specified periods of the collaboration. If AbbVie did not exercise one or more of its options, we would have incurred significant research and development expenses but would not receive any future option exercise, milestone payments, or royalty payments under the collaboration.

Such research and development activities shall be pursuant to plans agreed to by the parties and overseen by a joint governance committee, or JGC. Initially, we will have final decision-making authority within the JGC, subject to specified limitations. If AbbVie exercises its license option, however, AbbVie will assume final decision-making authority within the JGC. If AbbVie exercises its license option, it will also be solely responsible for all development and commercialization activities relating to compounds and products licensed pursuant to the agreement, and, at AbbVie's request, we could be required to effect a full transfer of the manufacturing process for such compound and products. Even if AbbVie does not exercise any of its options under the AbbVie Collaboration Agreement, we have agreed to grant AbbVie perpetual, exclusive or non-exclusive (as the case may be), worldwide licenses to certain know-how and patent rights developed by us or jointly by us and AbbVie arising from the collaboration.

AbbVie might not be effective in administering the JGC, obtaining approvals for the product candidates arising from our collaboration, or commercializing or manufacturing the resulting products. Further, AbbVie's objectives in connection with the collaboration may not be consistent with our best interests. AbbVie could use its leadership of the JGC or intellectual property it has licensed under the AbbVie Collaboration Agreement in a manner adverse to us, or it could halt, slow, or deprioritize its development and commercialization efforts under the collaboration. In any such instances, our business, financial condition, results of operations and prospects could be materially harmed.

We have only used the ClearPoint System to deliver our product. While other devices for delivery may be used in the future, any issues with the ClearPoint System or the manufacturer of the ClearPoint System, may result in delays in the development and commercialization of certain of our product candidates, which could have an adverse impact on our business.

The surgical approach that we are using for VY-AADC is similar, in some respects, to the stereotactic approach used for DBS. One primary difference with our approach is the ability to assist the physician in visualizing the delivery of VY-AADC to the putamen using real-time, intra-operative, MRI to avoid specific blood vessels to potentially reduce the risk of hemorrhages during the surgical procedure and to maximize the coverage of the putamen.

Investigators in the Phase 1b clinical trial of VY-AADC and the separate Phase 1 posterior trajectory trial used the real-time, intra-operative, MRI system called the ClearPoint System from MRIC. However, not all neuro-surgical units within the United States utilize this system and may employ other neuro-navigational systems that are not compatible with real-time MRI imaging. We intend to use the ClearPoint System at certain sites in our Phase 2-3 clinical trial and may choose to use it in future clinical trials of VY-AADC and any other of our product candidates that are injected directly into the brain. Therefore, any issues with the ClearPoint System, such as a finding that use of the ClearPoint System causes adverse events or a product recall, or the manufacturer of the ClearPoint System, such as bankruptcy or a decision to stop production of the system due to lack of profitability, could delay the development or commercialization of certain of our product candidates, including VY-AADC, as there currently is no other manufacturer of the ClearPoint System. To date, we are not aware of any other commercially available medical device that has been deemed substantially equivalent to the ClearPoint System. Outside the United States, the ClearPoint System is not widely available or utilized in neuro-surgical units.

Management of MRIC, the manufacturer of the ClearPoint System, has expressed substantial doubt as to the ability of MRIC to continue as a going concern on several occasions. As of March 31, 2018, MRIC reported cash and cash equivalents of \$7.5 million and secured debt (senior and junior) totaling approximately \$5.1 million on its balance sheet. MRIC also reported a net loss of \$1.6 million for the three months ended March 31, 2018.

We are developing a trajectory array guide device as our own real-time, intra-operative, MRI-compatible device that can be used with other neuro-navigational systems to dose VY-AADC and for other surgical procedures. We believe that the experience we have gained from delivering VY-AADC in our clinical trials to date and our work to develop the trajectory array guide device may inform AAV gene therapy delivery for our Huntington's disease program and other projects. In July 2018, we received 510(k) regulatory clearance of the trajectory array guide device from the Center for Devices and Radiological Health of the FDA. There are additional steps needed in making this device available for use including the manufacture of the product and compliance with state and Federal laws and regulations for medical devices.

We are currently exploring collaborations for the trajectory array guide device and expect to rely on third parties in the development and manufacture of the device. In May 2018, for example, we entered into a master services and supply agreement with MRIC which provides for MRIC to perform certain manufacturing, supply, development, and services as requested by us, including the supply of the ClearPoint System and cannula devices as well as to collaborate on the trajectory array guide device. Collaborations, including our collaboration with MRIC, are subject to risks similar to those described elsewhere in this "Risk Factors" section, and the corporate objectives of such current and potential future collaborators may not be consistent with our best interests. If we are unable to enter additional collaborations or any collaborations are not successful, use of the trajectory array guide device in our clinical trials could be adversely affected, and our clinical trials, including our pivotal Phase 2-3 clinical trial, could be delayed.

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

We will seek to enter into additional collaborations in the future, including sales, marketing, distribution, development, licensing, and/or broader collaboration agreements. Our likely collaborators include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies, and medical device manufacturers. However, we may not be able to enter into additional collaborations on favorable terms or at all.

Our ability to generate revenues from our collaborations will depend on our and our collaborators' abilities to successfully perform the functions assigned to each of us in these arrangements. In addition, our collaborators have the ability to abandon research or development projects and terminate applicable agreements. Moreover, an unsuccessful outcome in any clinical trial for which our collaborator is responsible could be harmful to the public perception and prospects of our gene therapy platform.

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

- collaborators have significant discretion in determining the amount and timing of the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- the preclinical studies and clinical trials conducted as part of these collaborations may not be successful;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on preclinical study or clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay preclinical studies and clinical trials, provide insufficient funding for preclinical studies and clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new preclinical studies or clinical trials or require a new formulation of a product candidate for preclinical studies or clinical trials;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates developed in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development of any product candidates, may cause delays or termination of the research, development or commercialization of such product candidates, may lead to additional responsibilities for us with respect to such product candidates or may result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- disputes may arise with respect to the ownership or inventorship of intellectual property developed pursuant to our collaborations;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- the terms of our collaboration agreement may restrict us from entering into certain relationships with other third parties, thereby limiting our options; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to the development or commercialization of product candidates in the most efficient manner, or at all. If our collaborations do not result in the successful development and commercialization of products, or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed, and we may need additional resources to develop our product candidates. Additionally, subject to its contractual obligations to us, if a collaborator of ours were to be involved in a business combination, it might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators, and the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization described in this periodic report also apply to the activities of our collaborators.

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

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, 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 fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our gene therapy platform. If we license rights to product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

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

We expect to rely on CROs and clinical trial sites to ensure our clinical trials are conducted properly and on time. We may also engage third parties such as clinical data management organizations, medical institutions and clinical investigators to conduct or assist in our clinical trials or other clinical development work. While we will have agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our third-party service providers' activities. Nevertheless, we will be responsible for ensuring that each of our clinical studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. Our reliance on these third-parties does not relieve us of our regulatory responsibilities. For example, our Phase 1b clinical trial of VY-AADC and our separate Phase 1 trial exploring the delivery of VY-AADC using a posterior trajectory are being conducted by four locations, including UCSF and UPMC. We expect to conduct the Phase 2 portion of our pivotal Phase 2-3 clinical program, at approximately twenty-four clinical trial sites (including neurosurgical and neurology patient referral sites). If any locations terminate the clinical trial, we would be required to find another party to conduct any new trials. We may be unable to find a new party to conduct new trials of our product candidates or obtain clinical supply of our product candidates or AAV vectors for such trials.

We and our third-party service providers are required to comply with the FDA's GCPs for conducting, recording and reporting the results of IND-enabling studies and clinical studies to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. We are also required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites at which the FDA may determine that our clinical trials did not comply with GCPs. If we or our third-party service providers fail to comply with applicable GCPs, the clinical data generated in our future clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving any marketing applications. In addition, our future clinical trials will require a sufficient number of patients to evaluate the safety and effectiveness of our product candidates. Accordingly, if we or our third-party service providers fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process. Failure to comply can also result in fines, adverse publicity, and civil and criminal sanctions.

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

Risks Related to Manufacturing

Gene therapies and their companion diagnostics are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in the development or commercialization of our product candidates or otherwise harm our business.

The manufacture of gene therapy products is technically complex, and necessitates substantial expertise and capital investment. Production difficulties caused by unforeseen events may delay the availability of material for our clinical studies. To meet the requirements of our current and planned future trials we have developed a proprietary manufacturing platform that provides a robust and scalable process for AAV production. We are using the baculovirus/Sf9 AAV production system, a technology for producing AAV gene therapy vectors at scale in insect-derived cells. The process has been successfully transferred to our contract manufacturing organizations where it is used in manufacturing clinical materials in accordance with the FDA's current good manufacturing practices, or cGMPs. We

have also built an onsite, state-of-the-art process research and development facility to enable the manufacturing of high quality AAV gene therapy vectors at laboratory scale.

We presently contract with third parties for the manufacturing of our program materials. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. The use of contracted manufacturing and reliance on collaboration partners is relatively cost efficient and has eliminated the need for our direct investment in manufacturing facilities and additional staff early in development. Although we rely on contract manufacturers, we have personnel with manufacturing and quality experience to oversee our contract manufacturers.

To date, our third-party manufacturers have met our manufacturing requirements for our program materials. We expect third-party manufacturers to be capable of providing sufficient quantities of our program materials to meet anticipated clinical trial scale demands. To meet our projected needs for commercial manufacturing, third parties with whom we currently work might need to increase their scale of production or we will need to secure alternate suppliers. We believe that there are alternate sources of supply for our program materials that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

To date, our third-party manufacturers have met our quality standards for our program materials. The manufacturers of pharmaceutical products must comply with strictly enforced cGMP requirements, state and federal regulations, as well as foreign requirements when applicable. Any failure of us or our contract manufacturing organizations to adhere to or document compliance to such regulatory requirements could lead to a delay or interruption in the availability of our program materials for clinical study. If we or our manufacturers were to fail to comply with the FDA, EMA, or other regulatory authority, it could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates. Our potential future dependence upon others for the manufacture of our product candidates may also adversely affect our future profit margins and our ability to commercialize any product candidates that receive regulatory approval on a timely and competitive basis.

Biological products are inherently difficult to manufacture. Our program materials are manufactured using technically complex processes requiring specialized equipment and facilities, highly specific raw materials, cells, and reagents, and other production constraints. Our production process requires a number of highly specific raw materials, cells, and reagents with limited suppliers. Even though we aim to have backup supplies of raw materials, cells, and reagents whenever possible, we cannot be certain they will be sufficient if our primary sources are unavailable. A shortage of a critical raw material, cell line, or reagent, or a technical issue during manufacturing may lead to delays in clinical development or commercialization plans. Any changes in the manufacturing of components of the raw materials we use could result in unanticipated or unfavorable effects in our manufacturing processes, resulting in delays.

Companion diagnostic devices may be required to diagnose a genetic disease or to determine patient antibody levels to certain components in a product, and could also require a sophisticated, technically complex manufacturing processes. If we or our contract manufacturing organizations fail to manufacture such diagnostics or comply with relevant regulatory requirements or approvals, we might seek to transition such manufacturing processes to another contract manufacturing organization. We might not be able to transition such processes in a timely manner or at all, and our commercialization and development efforts could be delayed.

Delays in obtaining regulatory approval of our or our collaborators' manufacturing process and facility or disruptions in our manufacturing process may delay or disrupt our commercialization efforts. Until recently, no cGMP gene therapy manufacturing facility in the United States had received approval from the FDA for the manufacture of an approved gene therapy product.

Before we can begin to commercially manufacture our product candidates in our own facility, or the facility of a collaborator, we must obtain regulatory approval from the FDA for our manufacturing process and our collaborator's facility. A manufacturing authorization must also be obtained from the appropriate European Union regulatory authorities. Until recently, no cGMP gene therapy manufacturing facility in the United States had received approval from

the FDA for the manufacture of an approved gene therapy product and, therefore, the timeframe required for us to obtain such approval is uncertain. In addition, we must pass a pre-approval inspection of our or our collaborator's manufacturing facility by the FDA and other relevant regulatory authorities 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 cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any of our vendors, contract laboratories or suppliers is found to be out of compliance with cGMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop.

Failure to comply with ongoing regulatory requirements could cause us to suspend production or put in place costly or time-consuming remedial measures.

The regulatory authorities may, at any time, following approval of a product for sale, audit the manufacturing facilities for such product, or institute biennial inspections. If any such inspection or audit identifies a failure to comply with applicable regulations, or if a violation of product specifications or applicable regulations occurs independent of such an inspection or audit, the relevant regulatory authority may require remedial measures that may be costly or time-consuming to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a manufacturing facility. Any such remedial measures imposed upon our third-party manufacturers or us could harm our business, financial condition, results of operations and prospects.

If our third-party manufacturers or we fail to comply with applicable cGMP regulations, FDA and foreign regulatory authorities can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate or suspension or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition, results of operations and prospects to be harmed.

Additionally, if supply from any third-party manufacturers is delayed or interrupted, there could be a significant disruption in the supply of our clinical or commercial material. We have agreements in place with our contract manufacturers pursuant to which we are collaborating on cGMP manufacturing processes and analytical methods for the manufacture of our AAV product candidates. Therefore, if we are unable to enter into an agreement with our contract manufacturers to manufacture clinical or commercial material for our product programs beyond VY-AADC, or if our agreement with our contract manufacturers were terminated, we would have to find suitable alternative manufacturers. This could delay our or our collaborators' ability to conduct clinical trials or commercialize our current and future product candidates. The regulatory authorities also may require additional trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and could result in a delay in our desired clinical and commercial timelines.

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

Given the nature of biologics manufacturing, there is a risk of contamination. Any contamination could adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage.

Some of the raw materials required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. 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 commercial manufacturing or the production of clinical material, which could adversely affect our development timelines and our business, financial condition, results of operations and prospects.

Interruptions in the supply of product candidates or inventory loss may harm our operating results and financial condition.

Our product candidates are manufactured using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints. The complexity of these processes, as well as strict government standards for the manufacture and storage of our product candidates, subjects us to manufacturing risks. While product candidate batches released for use in clinical trials or for commercialization undergo sample testing, some defects may only be identified following product release. In addition, process deviations or unanticipated effects of approved process changes may result in these intermediate products not complying with stability requirements or specifications. Our product candidates must be stored and transported at temperatures within a certain range. If these environmental conditions deviate, our product candidates' remaining shelf-lives could be impaired or their efficacy and safety could be negatively impacted, making them no longer suitable for use.

The occurrence, or suspected occurrence, of manufacturing and distribution difficulties can lead to lost inventories and, in some cases, product recalls, with consequential reputational damage and the risk of product liability. The investigation and remediation of any identified problems can cause production delays, substantial expense, lost sales and delays of new product launches. Any interruption in the supply of finished products or the loss thereof could hinder our ability to timely distribute our products and satisfy customer demand. Any unforeseen failure in the storage of the product or loss in supply could delay our clinical trials and, if our product candidates are approved, result in a loss of our market share and negatively affect our business, financial condition, results of operations and prospects.

Risks Related to Our Business Operations

We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates that may be a greater commercial opportunity, or for which there is a greater likelihood of success.

The success of our business depends upon our ability to identify, develop and commercialize product candidates generated through our gene therapy platform. Research programs to identify new product candidates require substantial technical, financial and human resources. Although VY-AADC is currently in clinical development and our other product candidates are in preclinical development, we may fail to identify other potential product candidates for clinical development for several reasons. For example, our research may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects, may be commercially impracticable to manufacture or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

Additionally, because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our spending on current and future research and development programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Alternatively, we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate or fail to develop a potentially successful product candidate, which could harm our business, financial condition, results of operations and prospects.

Our future success depends on our ability to retain key members of our management team, and to attract, retain and motivate qualified personnel.

We are highly dependent on the management, technical, and scientific expertise of principal members of our management, scientific, and clinical teams including our former President and Chief Executive Officer, Steven M. Paul, M.D., who now serves as a senior advisor, director, and member of our Science and Technology Committee, and G.

Andre Turenne, who joined us as President and Chief Executive Officer in July 2018. While we have entered into employment agreements or offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are “at will” employees. We currently do not have “key person” insurance on any of our employees. The loss of the services of one or more of our current employees might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel is also critical to our success. There currently is a shortage of skilled individuals with substantial gene therapy experience, which is likely to continue. As a result, competition for skilled personnel, including in gene therapy research and vector manufacturing, is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms, if at all, given the competition among numerous pharmaceutical and biotechnology companies and academic institutions for individuals with similar skill sets. 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. In addition, failure to succeed in preclinical or clinical trials or applications for marketing approval may make it more challenging to recruit and retain qualified personnel. The inability to recruit, or loss of services of certain executives, key employees, consultants or advisors, may impede the progress of our research, development and commercialization objectives and could harm our business, financial condition, results of operations and prospects.

If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer.

If we are successful in executing our business strategy, we will need to expand our managerial, operational, financial and other systems and resources to manage our operations, continue our research and development activities and, in the longer term, build a commercial infrastructure to support commercialization of any of our product candidates that are approved for sale. We can provide no assurances that we will have sufficient resources in the future to manage all of our planned programs. Future growth would impose significant added responsibilities on members of management, may lead to significant added costs, and may divert our management and business development resources. It is likely that our management, finance, development personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and product candidates requires that we continue to develop more robust business processes and improve our systems and procedures in each of these areas and to attract and retain sufficient numbers of talented employees. We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development and growth goals.

Our employees, principal investigators, consultants and commercial partners 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 FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, 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 restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, 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 government 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, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be 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, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, which we refer to, collectively, as the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing,

review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. In May 2017, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017. Thereafter, the Senate Republicans introduced and then updated a bill to replace the ACA known as the Better Care Reconciliation Act of 2017. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a “skinny” version of the Better Care Reconciliation Act of 2017. In addition, the Senate considered proposed healthcare reform legislation known as the Graham-Cassidy bill. None of these measures was passed by the U.S. Senate.

With enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

The current administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Trump Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Trump Administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. 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 candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

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

Under the CURES Act and the Trump Administration's regulatory reform initiatives, the FDA's policies, regulations and guidance may be revised or revoked and that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.

In December 2016, the CURES Act was signed into law. The CURES Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. An under-staffed FDA could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. Moreover, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations, however it is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

We may be subject, directly or indirectly, to federal, state, and foreign healthcare laws and regulations, including fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state laws and regulations, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims act, and the Physician Payments Sunshine Act and regulations. These laws will impact, among other things, our proposed sales, marketing and educational programs. In addition, we may be subject to data privacy laws by both the federal government and the states in which we conduct our business. Such laws that may

constrain the business or financial arrangements and relationships through which we conduct our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for either the referral of an individual for, or the purchase, recommendation, leasing or furnishing of, an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other. Further, the ACA amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it;
- the federal civil and criminal false claims laws and civil monetary penalty laws, including the civil False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other government payors 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 ACA provided and recent government cases against pharmaceutical and medical device manufacturers support the view that federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, may implicate the civil False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit a person from knowingly and willfully executing or attempting to execute a scheme or from making false or fraudulent statements to defraud any healthcare benefit program, regardless of the payor (e.g., public or private);
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, and as amended again by the final HIPAA omnibus rule, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to HIPAA, published in January 2013, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses and health care providers;
- federal transparency laws, including the federal Physician Payments Sunshine Act, which is part of the ACA, that requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to Center for Medicare & Medicaid Services, or CMS, information related to payments and other transfers of value provided to physicians and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members, by the 90th day of each subsequent calendar year, and disclosure of such information is made by CMS on a publicly available website; and
- state and/or foreign law equivalents of each of the above federal laws, such as state anti-kickback and false claims laws that may apply to arrangements and claims involving health care items or services reimbursed by non-governmental third-party payors; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts in certain circumstances, such as specific disease states.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, imprisonment and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities.

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 face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and may face an even greater risk if we commercialize any products that we may develop. 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;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend the related litigation;
- withdrawal of clinical trial participants;

- the inability to commercialize any product candidates that we may develop; and
- injury to our reputation and significant negative media attention.

Although we maintain product liability insurance coverage in the amount of \$5.0 million per occurrence and \$5.0 million in the aggregate, this insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial 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.

If we, our collaborators, or any third-party manufacturers engaged by us or our collaborators fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We, our collaborators, and any third-party manufacturers we engage are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the generation, handling, use, storage, treatment, manufacture, transportation and disposal of, and exposure to, hazardous materials and wastes, as well as laws and regulations relating to occupational health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biologic and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain general liability insurance and workers' compensation insurance for certain costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could harm our business, financial condition, results of operations and prospects.

Further, with respect to the operations of any current or future collaborators or third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products.

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. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the most recent global financial crisis, 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. This is particularly true in the European Union, which is recovering from a severe economic crisis. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payors or our collaborators. 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.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a 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 clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Although we maintain cyber risk insurance for certain costs we may incur due to a cyber related event, this insurance may not provide adequate coverage against potential liabilities. Additionally, 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 delayed.

Risks Related to the Commercialization of Our Product Candidates

The affected populations for our product candidates may be smaller than we or third parties currently project, which may affect the addressable markets for our product candidates.

Our projections of the number of people who have the diseases we are seeking to treat, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are estimates based on our knowledge and understanding of these diseases. The total addressable market opportunity for our product candidates will ultimately depend upon a number of factors including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient access and product pricing and reimbursement. Prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward-looking and speculative. The process we have used in developing an estimated prevalence range for the indications we are targeting has involved collating limited data from multiple sources. While we believe these sources are reliable, we have not independently verified the data. Accordingly, the prevalence estimates included in our periodic reports and other reports filed with or furnished to the SEC should be viewed with caution. Further, the data and statistical information used in such reports, including estimates derived from them, may differ from information and estimates made by our competitors or from current or future studies conducted by independent sources.

The use of such data involves risks and uncertainties and is subject to change based on various factors. Our estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of the diseases we seek to address. The number of patients with the diseases we are targeting in the United States, the European Union and elsewhere may turn out to be lower than expected or may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or access, all of which would harm our results of operations and our business.

If we are unable to establish sales, medical affairs and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any product revenue.

We have recently begun to build our sales and marketing organization. To successfully commercialize any products that may result from our clinical development programs, we will need to further develop these capabilities, either on our own or with others. The establishment and development of our own commercial team or the establishment of a contract sales force to market any products we may develop will be expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability.

Under our collaboration agreement with Sanofi Genzyme, Sanofi Genzyme has an exclusive option to license, develop and commercialize ex-U.S. rights to our Friedreich's ataxia program, a future program to be designated by Sanofi Genzyme and our Huntington's disease program. Additionally, we have granted Sanofi Genzyme an incremental

option to co-commercialize our Huntington's disease program in the United States and to acquire worldwide rights to our spinal muscular atrophy program. If Sanofi Genzyme exercises any of these options, we would be eligible to receive specified option fees. In addition, we would be eligible to receive specified milestone payments and royalties for any product developed in such programs.

Under our collaboration and option agreement with AbbVie, AbbVie has options to advance certain compounds into further development and to obtain an exclusive, worldwide license, with the right to sublicense, under certain of our intellectual property rights to develop and commercialize such compounds and corresponding products for all human diagnostic, prophylactic and therapeutic uses. If AbbVie exercises any of these options, we would be eligible to receive specified option fees. In addition, we would be eligible to receive specified development and regulatory milestone payments and tiered royalties on the global commercial net sales products developed under our collaboration.

In the future, we may enter into collaborations regarding other of our product candidates with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any current or future collaborators do not commit sufficient resources to commercialize our products, or we are unable to develop the necessary capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We compete with many companies that currently have extensive, experienced and well-funded medical affairs, marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates. We might face unforeseen costs and expenses associated with creating an independent sales and marketing organization. Our sales personnel might also face difficulties obtaining access to physicians or being able to persuade adequate numbers of physicians to use or prescribe our products or selling our products if we lack complementary products, which could disadvantage us compared to companies with more extensive product lines. Without an internal team or the support of a third-party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our potential products. If any of our product candidates is approved but fails to achieve market acceptance among physicians, patients, or third-party payors, we will not be able to generate significant revenues from such product, which could harm our business, financial condition, results of operations and prospects.

The 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.

We expect the cost of a single administration of gene therapy products, such as those we are developing, to be substantial, when and if they achieve regulatory approval. 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 our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of 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. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient and the indication;
- convenient and easy-to-administer compared to alternative treatments;

- cost-effective compared to alternative treatments; and
- neither experimental nor investigational.

No uniform policy requirement for coverage and reimbursement for biopharmaceutical products exists among third-party payors. Therefore, coverage and reimbursement for such products can differ significantly from payor to payor. As a result, obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to each different payor supporting scientific, clinical and cost-effectiveness data. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment including our research, development, manufacture, sales, and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement is critical to new product acceptance. Additionally, there may be significant delays in obtaining coverage and reimbursement for newly approved drugs and biologics, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities.

There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. In the United States, third-party payors, including government payors such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare and Medicaid programs increasingly are used as models for how private payors and government payors develop their coverage and reimbursement policies. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products.

The CMS is responsible for determining whether a product should be approved for coverage and reimbursement under the Medicare program. It is difficult to predict what CMS will decide with respect to coverage and reimbursement for novel products such as ours, as there is no body of established practices and precedents for these types of products. Currently, no gene therapy product has been approved for coverage and reimbursement by the CMS. Moreover, reimbursement agencies in the European Union may be more conservative than CMS. For example, several cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European Union Member States. It is difficult to predict what third-party payors will decide with respect to the coverage and reimbursement for our product candidates, especially given that the cost of our product candidates is likely to be very high and pricing of such products is highly uncertain.

Outside the United States, international operations generally are subject to extensive government price controls and other market regulations, and increasing emphasis on cost-containment initiatives in the European Union, Canada and other countries may put pricing pressure on us. For example, one gene therapy product was approved in the European Union in 2012 but is yet to be widely available commercially. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable product revenues.

Moreover, increasing efforts by government and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. Payors increasingly are considering new metrics as the basis for reimbursement rates, such as average sales price, or ASP, average manufacturer price, or AMP, and Actual Acquisition Cost. The existing data for reimbursement based on some of these metrics is relatively limited, although certain states have begun to survey acquisition cost data for the purpose of setting Medicaid reimbursement rates, and CMS has begun making pharmacy National Average Drug Acquisition Cost and National Average Retail Price data publicly available on at least a monthly basis. The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug and device products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. 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. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Therefore, it is difficult to project the impact of these evolving reimbursement metrics on the willingness of payors to cover candidate products that we or our partners are able to commercialize. 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 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 intense. As a result, increasingly high barriers are being erected to the entry of new products such as ours.

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 the FDA in the United States, EMA in the European Union 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 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 or the European Commission, or other regulatory authorities;
- patient awareness of, and willingness to seek, genotyping;
- the willingness of physicians to prescribe new therapies;

- the willingness of physicians to undergo specialized training with respect to administration of our product candidates;
- 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 or restrictions on the use of our products together with other medications;
- 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 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.

Our gene therapy approach utilizes vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology, with three gene therapy products approved to date in the United States and only two gene therapy products approved to date in the European Union, of which one is no longer available commercially. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our product candidates, prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death seen in other trials using non-AAV gene therapy vectors. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

If we obtain approval to commercialize our product candidates outside of the United States, in particular in the European Union, a variety of risks associated with international operations could harm our business.

We expect that we will be subject to additional risks in commercializing our product candidates outside the United States, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;

- reduced or loss of protection under our intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability; and
- greater difficulty with enforcing our contracts in jurisdictions outside of the United States.

We must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In many foreign countries, it is common for others to engage in business practices that are prohibited by U.S. laws and regulations applicable to us, including the FCPA. In addition, the FCPA presents particular challenges in the pharmaceutical industry because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Although we expect to implement policies and procedures designed to comply with these laws and policies, there can be no assurance that our employees, contractors and agents will comply with these laws and policies. If we are unable to successfully manage the challenges of international expansion and operations, our business and operating results could be harmed.

Risks Related to Our Intellectual Property

Our rights to develop and commercialize our product candidates are subject to, in part, the terms and conditions of licenses granted to us by others.

We are reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our technology and products, including technology related to our manufacturing process and our product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses. These licenses may also require us to grant back certain rights to licensors and to pay certain amounts relating to sublicensing patent and other rights under the agreement.

In some circumstances, particularly in-licenses with academic institutions, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce or defend the patents, covering technology that we license from third parties. Therefore, we cannot be certain that these patents and applications will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If our licensors fail to maintain such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In certain circumstances, we have or may license technology from third parties on a non-exclusive basis. In such instances, other licensees may have the right to enforce our licensed patents in their respective fields, without our oversight or control. Those other licensees may choose to enforce our licensed patents in a way that harms our interest, for example, by advocating for claim interpretations or agreeing on invalidity positions that conflict with our positions or our interest. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we own or may own in the future.

Further, in many of our license agreements we are responsible for bringing any actions against any third party for infringing on the patents we have licensed. Certain of our license agreements also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products and minimum yearly diligence obligations in developing and commercializing the product. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship or ownership of inventions and know-how resulting from the creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

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.

If we fail to comply with our obligations under these license agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to develop, manufacture, or market products covered by the license or may face other penalties under the agreements. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

Furthermore, the research resulting in certain of our licensed patent rights and technology was funded by the U.S. government. As a result, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with U.S. government funding, the U.S. government generally obtains certain rights in any resulting patents, including a non-exclusive, royalty-free license authorizing the U.S. government, or a third party on its behalf, to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The U.S. government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government, or a third party on its behalf, of such rights could harm our competitive position, business, financial condition, results of operations and prospects.

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 of sufficient breadth, 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 success depends, in large part, on our and our licensors' ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates and manufacturing technology. We and our licensors have sought, and we intend to seek in the future, to protect our proprietary position by filing patent applications in the United States and abroad related to many of our technologies and product candidates that are important to our business.

The patent prosecution process is expensive, time-consuming and complex, and we may not have and may not in the future be able to file, prosecute, maintain, enforce, defend or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. For example, in some cases, the work of certain academic researchers in the gene therapy field has entered the public domain, which may compromise our ability to obtain patent protection for certain inventions related to or building upon such prior work. Consequently, we may not be able to obtain any such patents to prevent others from using our technology for, and developing and marketing competing products to treat, these indications. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent 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. As a result, the issuance, scope, validity, enforceability and commercial value of our and our licensors' patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. In particular, during prosecution of any patent application, the issuance of any patents based on the application may depend upon our ability to generate additional preclinical or clinical data that support the patentability of our proposed claims. We may not be able to generate sufficient additional data on a timely basis, or at all. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our and our licensors' patent protection.

We may not be aware of all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all.

Therefore, we cannot be certain that we, or a licensor, were the first to make the inventions claimed in any owned or any licensed patents or pending patent applications, respectively, or which entity was the first to file for patent protection until such patent application publishes or issues as a patent. Databases for patents and publications, and methods for searching them, are inherently limited, so it is not practical to review and know the full scope of all issued and pending patent applications. As a result, the issuance, scope, validity, enforceability, and commercial value of our and our licensed patent rights are uncertain.

Even if the patent applications we license or may own in the future do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability may be challenged in the courts and patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology, resulting in termination of our access to such intellectual property, or increase our financial or other obligations to our licensors.

The agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, result in loss of access, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could harm our business, financial condition, results of operations and prospects.

We may not be successful in obtaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to certain intellectual property, through licenses from third parties, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for our product candidates. 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.

We sometimes collaborate with non-profit and academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to develop our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business significantly.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the United States Patent and Trademark Office, or USPTO, and various government patent agencies outside of the United States over the lifetime of our licensed patents and/or applications and any patent rights we may own in the future. We rely on our outside counsel or our licensing partners to pay these fees due to patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance 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. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business.

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. Our intellectual property rights may vary from country to country and foreign protections could be less extensive than those in the United States. 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. 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, further, may export otherwise 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 or methods of treatment, 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, an April 2014 report from the Office of the United States Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. 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.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court. We may not be able to protect our trade secrets in court.

If one of our licensing partners or we initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, lack of written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that an individual connected with prosecution of the patent, including an inventor, an employee of the company, a collaborator or advisor, withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include pre-issuance submissions, *ex parte* re-examination, post-grant review, *inter partes* review and equivalent proceedings in foreign jurisdictions. Some of these mechanisms may even be exploited anonymously by third parties. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose part or, all of the patent protection on one or more of our product candidates. Such a loss of patent protection could harm our business.

In addition to the protection afforded by patents, we rely on trade secret protection, nondisclosure, and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. Some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, collaborators, contractors, and other third parties. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could harm 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 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 complex litigation regarding patents and other intellectual property rights. We may become party to, or threatened with, infringement litigation claims regarding our products and technology, including claims from competitors or from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may have no deterrent effect. Moreover, we may become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including *ex parte* re-examination, post grant review and *inter partes* review before the USPTO or foreign patent offices. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of the merit of the claim. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could adversely affect our ability to commercialize our product candidates or any other of our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such asserted third-party U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to

present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Similar challenges exist in other jurisdictions. If we are found to infringe a third-party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third-party to continue developing, manufacturing and marketing our product candidates and technology. However, we may not be able to obtain any required 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 and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidates. 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 or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our product candidates or force us to cease some of our business operations, which could harm our business. In addition, we may be forced to redesign our product candidates, seek new regulatory approvals, and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, reputation, financial condition, results of operations and prospects.

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

Competitors may infringe our intellectual property rights or the intellectual property rights of our licensing partners, or we may be required to defend against claims of infringement. To counter infringement or unauthorized use claims or to defend against claims of infringement can be expensive and time consuming. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could adversely affect our ability to compete in the marketplace.

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 are currently, or were previously, employed at universities 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. 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.

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

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

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes several significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and also may affect patent litigation. These also include provisions that switched the United States from a “first-to-invent” system to a “first-inventor-to-file” system, allow third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent by the USPTO administered post grant proceedings. Under a first-inventor-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO has promulgated regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-inventor-to-file provisions, only became effective on March 16, 2013. The Leahy-Smith Act could result in an increased investment in filing applications earlier, increase the uncertainties and costs surrounding the prosecution of our patent applications, and increase the enforcement or defense of our issued patents, all of which could harm our business, financial condition, results of operations and prospects.

As an example, the Leahy-Smith Act provides a new administrative tribunal known as the Patent Trial and Appeals Board, or PTAB, that provides a venue for companies to challenge the validity of competitor patents at a cost that is much lower than district court litigation and on timelines that are much faster. Although it is not clear what, if any, long-term impacts the PTAB proceedings will have on the operation of our business, the initial results of patent challenge proceedings before the PTAB since its inception in 2013 have resulted in the invalidation of many U.S. patent claims. The availability of the PTAB as a lower-cost, faster and potentially more potent tribunal for challenging patents could therefore increase the likelihood that our own licensed patents will be challenged, thereby increasing the uncertainties and costs of maintaining and enforcing them. Moreover, if such challenges occur, we may not have the right to control the defense. In certain situations, we may be required to rely on our licensor to consider our suggestions and to defend such challenges, with the possibility that it may not do so in a way that best protects our interests.

We also may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in other contested proceedings such as opposition, derivation, reexamination, *inter partes* review, or post-grant review proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future products.

The patent positions of companies engaged in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Two cases involving diagnostic method claims and “gene patents” have recently been decided by the Supreme Court of the United States, or Supreme Court. On March 20, 2012, the Supreme Court issued a decision in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, or *Prometheus*, a case involving patent claims directed to a process of measuring a metabolic product in a patient to optimize a drug dosage for the patient. According to the Supreme Court, the addition of well-understood, routine or conventional activity such as “administering” or “determining” steps was not enough to transform an otherwise patent-ineligible natural phenomenon into patent-eligible subject matter. On July 3, 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should

be rejected as directed to not patent-eligible subject matter. On June 13, 2013, the Supreme Court issued its decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, or *Myriad*, a case involving patent claims held by Myriad Genetics, Inc. relating to the breast cancer susceptibility genes BRCA1 and BRCA2. In *Myriad*, the Supreme Court held that an isolated segment of naturally occurring DNA, such as the DNA constituting the BRCA1 and BRCA2 genes, is not patent eligible subject matter, but that complementary DNA, which is an artificial construct that may be created from RNA transcripts of genes, may be patent eligible.

On March 4, 2014, the USPTO issued a guidance memorandum to patent examiners titled 2014 Procedure for Subject Matter Eligibility Analysis of Claims Reciting or Involving Laws of Nature/Natural Principles, Natural Phenomena, and/or Natural Products. These guidelines and more recent guidelines superseding them instruct USPTO examiners on the ramifications of the *Prometheus* and *Myriad* rulings and apply the *Myriad* ruling to natural products and principles including all naturally occurring nucleic acids. Patents for certain of our product candidates contain claims related to specific DNA sequences that are naturally occurring and, therefore, could be the subject of future challenges made by third parties. In addition, the recent USPTO guidance could make it impossible for us to pursue similar patent claims in patent applications we may prosecute in the future.

We cannot assure you that our efforts to seek patent protection for our technology and products will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact the Supreme Court's decisions in *Prometheus* and *Myriad* may have on the ability of life science companies to obtain or enforce patents relating to their products and technologies in the future. These decisions, the guidance issued by the USPTO and rulings in other cases or changes in USPTO guidance or procedures could have an adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Moreover, although the Supreme Court has held in *Myriad* that isolated segments of naturally occurring DNA are not patent-eligible subject matter, certain third parties could allege that activities that we may undertake infringe other gene-related patent claims, and we may deem it necessary to defend ourselves against these claims by asserting non-infringement and/or invalidity positions, or paying to obtain a license to these claims. In any of the foregoing or in other situations involving third-party intellectual property rights, if we are unsuccessful in defending against claims of patent infringement, we could be forced to pay damages or be subjected to an injunction that would prevent us from utilizing the patented subject matter. Such outcomes could harm our business, financial condition, results of operations or prospects.

Outside the United States, other courts have also begun to address the patenting of genetic material. In August 2015, the Australian High Court ruled that isolated genes cannot be patented in Australia. The decision did not address methods of using genetic material. Any ruling of a similar scope in other countries could affect the scope of our intellectual property rights.

If we do not obtain patent term extension and data exclusivity for our product candidates, our business may be harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of our product candidates, one or more of our U.S. patents, which may cover non-gene therapy compounds, may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended per FDA-approved product, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Further, certain of our licenses currently or in the future may not provide us with the right to control decisions the licensor or its other licensees on Orange Book listings or patent term extension decisions under the Hatch-Waxman Act. Thus, if one of our important licensed patents is eligible for a patent term extension under the Hatch-Waxman Act, and it covers a product of another licensee in addition to our own product candidate, we may not be able to obtain that extension if the other licensee seeks and obtains that extension first. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within

applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time-period or the scope of patent protection afforded during any such extension could be less than we request. If we are unable to obtain patent term extension or the scope of term of any such extension is less than we request, the period during which we will have the right to exclusively market our product may be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be materially reduced.

If our trademarks and trade name are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We own service mark registrations in the USPTO for the marks “VOYAGER THERAPEUTICS” and “VOYAGER THERAPEUTICS Logo” and pending trademark applications in the USPTO relating to our trajectory array guide device for the marks “V-TAG” and the “V-TAG Logo” as well as a pending trademark application in the European Community for “V-TAG”. Our trademarks or our trade name may be challenged, infringed, circumvented or declared generic or found to infringe prior third-party marks. We may not be able to protect our rights in our trademarks or in our trade name, which we need in order to build name recognition among potential partners or customers in our markets of interest. It is possible that competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of prior registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade name. Over the long term, if we are unable to establish name recognition based on our trademarks and trade name, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce and protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights and other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and such rights may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make gene therapy products that are similar to our product candidates but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and
- we may choose not to file a patent for certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

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

Because we currently rely on certain third parties to manufacture all or part of our product candidates and to perform quality testing, and because we collaborate with various organizations and academic institutions for the advancement of our gene therapy platform and pipeline, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may harm our business, financial condition, results of operations and prospects.

Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets by third parties. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business, financial condition, results of operations and prospects.

Risks Related to Ownership of Our Common Stock

Our executive officers, directors, principal stockholders and their affiliates exercise significant influence over our company.

The holdings of our executive officers, directors, principal stockholders and their affiliates, including investment funds affiliated with Third Rock Ventures, investment funds affiliated with Fidelity Management Research Company, or Fidelity, and investment funds affiliated with BB Biotech AG represent beneficial ownership, in the aggregate, of approximately 45% of our outstanding common stock as of June 30, 2018. As a result, these stockholders, if they act together, will be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

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

Our shares of common stock began trading on the Nasdaq Global Select Market on November 11, 2015. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of our stockholders to sell their shares.

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 will rely in part on the research and reports that industry or financial analysts publish about us or our business. If no or few analysts maintain coverage of us, the trading price of our stock would likely decrease. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our stock incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, and, in any event, we have filed a registration statement permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline. In addition, we have registered on a registration statement on Form S-3 that has been declared effective, the sale of up to \$250.0 million in aggregate of an indeterminate number of shares of common stock and preferred stock, an indeterminate principal amount of debt securities, and an indeterminate number of warrants. In November 2017, under such shelf registration statement, we issued and sold 5,175,000 shares of common stock to the public at an offering price of \$12.00 per share, including 675,000 shares of common stock issued upon the full exercise by the underwriter of their option to purchase additional shares, resulting in net proceeds of \$58.0 million after deducting underwriting discounts, commissions, and offering expenses payable by us. The registration statement also registers the offering, issuance, and sale of common stock having up to a maximum aggregate offering price of \$75.0 million that we may issue and sell in an at-the-market offering under a sales agreement we entered into with Cowen and Company, LLC on December 1, 2016 pursuant to a sales agreement prospectus that forms a part of the registration statement. As of June 30, 2018, approximately \$75.0 million in shares of common stock remain eligible for sale under the sales agreement.

Certain holders of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Any sales of securities by these stockholders could have a material adverse effect on the trading price of 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.

The price of our common stock is likely to be volatile and may fluctuate substantially. From April 1, 2018 through June 30, 2018, the sales price of our common stock ranged from a high of \$24.24 to a low of \$16.40 on the Nasdaq Global Select Market. As a result of this volatility, our stockholders may not be able to sell their common stock

at or above the price at which they purchased it. The market price for our common stock may be influenced by many factors, including:

- our success in commercializing any product candidates for which we obtain marketing approval;
- regulatory action and results of clinical trials of our product candidates or those of our competitors;
- the success of competitive products or technologies;
- the results of clinical trials of our product candidates;
- the results of clinical trials of product candidates of our competitors;
- the commencement, termination, and success of our collaborations;
- regulatory or legal developments in the United States and other countries;
- 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 technologies, the cost of commercializing such product candidates, and the cost of development of any such product candidates or technologies;
- 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;
- the ability to secure third-party reimbursement for our product candidates;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section and elsewhere in this Quarterly Report on Form 10-Q.

If our operating results fall below the expectations of investors or securities analysts for a given period, the price of our common stock could decline substantially. Furthermore, any fluctuations in our operating results from period to period may, in turn, cause the price of our stock to fluctuate substantially. We believe that such comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation often has been instituted against that company. We also may face securities class-action litigation if we cannot obtain regulatory approvals for or if we otherwise fail to commercialize our product candidates. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

We have broad discretion in how we apply our available funds, and we may not use these funds effectively, which could affect our results of operations and cause our stock price to decline.

Our management will have broad discretion in the application of our existing cash, cash equivalents and marketable securities and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply our available funds effectively could result in financial losses that could cause the price of our common stock to decline and delay the development of our product candidates and preclinical programs. Pending their use, we may invest our available funds in a manner that does not produce income or that loses value.

We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

For so long as we remain an “emerging growth company,” or EGC, as defined in the JOBS Act, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act of 2002;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these exemptions until we are no longer an EGC. We would cease to be an EGC upon the earlier of: (i) the last day of the fiscal year in which we have total annual gross revenue of \$1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of our IPO, which is December 31, 2020; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission or SEC, which means the first day of the year following the first year in which the market value of our common stock that is held by non-affiliates exceeds \$700.0 million as of June 30th.

We expect to continue to take advantage of some, but not all, of the available exemptions. In particular, we have not included all of the executive compensation information that would be required if we were not an EGC. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions.

In addition, the JOBS Act provides that an EGC may take advantage of an extended transition period for complying with new or revised accounting standards. This allows an EGC to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile and may decline.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an EGC, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002,

the Dodd-Frank Wall Street Reform and Consumer Protection Act, and rules subsequently implemented by the SEC and The Nasdaq Stock Market have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly. For example, these rules and regulations have made it more difficult and more expensive for us to obtain director and officer liability insurance, and we have been required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Provisions in our amended and restated certificate of incorporation and bylaws and 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 bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions also could 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 such that only one of three classes of members of the board is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a stockholder rights plan, or so-called “poison pill,” that would work to dilute the stock

ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our amended and restated certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, 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.

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 or employees.

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 (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws or (iv) 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. 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 a stockholder's ability to bring a claim in a judicial forum that he, she or it finds favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees 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 the State of 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 which could have a material adverse effect on our business, financial condition or results of operations.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

ITEM 5. OTHER INFORMATION

Effective August 2, 2018, we entered into a consulting agreement, or the Paul Agreement, with Steven M. Paul, M.D., our former President and Chief Executive Officer, pursuant to which Dr. Paul has agreed to provide consulting and advisory services to us, including but not limited to scientific guidance in connection with the certain of the Company's collaborations, research and development programs, and business development efforts, generally one day per week for a twelve-month period commencing on August 2, 2018. We refer to such service period, as the same may be extended or shortened by the parties as further described below, as the Term.

Under the Paul Agreement, Dr. Paul will receive compensation including \$16,700 in consulting fees per month, not to exceed \$200,500 during the Term without our express written consent. We will also reimburse Dr. Paul for pre-approved expenses incurred in connection with Dr. Paul's provision of services under the Paul Agreement. The Paul Agreement also provides for, among other things, confidentiality obligations and assignment covenants applicable to Dr. Paul, which continue beyond the Term.

The Paul Agreement may be terminated prior to its expiration (i) by us immediately at any time upon written notice to Dr. Paul if Dr. Paul materially breaches the Paul Agreement, the Retirement Agreement, dated June 28, 2018, by and between us and Dr. Paul, which we refer to as the Retirement Agreement, or the Restrictive Covenants Agreement referenced within the Retirement Agreement; (ii) by Dr. Paul at any time immediately upon written notice if we materially breach the Paul Consulting Agreement or the Retirement Agreement; (iii) by either party at any time, for any reason or no reason, with not less than forty-five (45) days prior written notice to the other party; (iv) at any time upon the mutual written consent of both parties; or (v) automatically upon the death, physical incapacitation or mental incompetence of Dr. Paul.

ITEM 6. EXHIBITS

The exhibits filed or furnished as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index, which is incorporated herein by reference.

INDEX TO EXHIBITS

Exhibit No.	Description	Incorporated by Reference to:				
		Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number	Filed Herewith
10.1	Third Amendment to Lease Agreement, by and between Voyager Therapeutics, Inc. and UP 45/75 Sidney Street, LLC, dated June 1, 2018.	8-K	10.1	6/5/2018	001-37625	
10.2	First Amendment to Lease Agreement, by and between Voyager Therapeutics, Inc. and UP 64 Sidney Street, LLC, dated June 1, 2018.	8-K	10.2	6/5/2018	001-37625	
10.3	Retirement Agreement, by and between Voyager Therapeutics, Inc. and Steven M. Paul, dated June 28, 2018.	8-K	10.1	6/29/2018	001-37625	
10.4	Employment Agreement, by and between Voyager Therapeutics, Inc. and G. Andre Turenne, dated June 28, 2018.	8-K	10.2	6/29/2018	001-37625	
10.5	Consulting Agreement, by and between Voyager Therapeutics, Inc. and Steven M. Paul, M.D., dated August 2, 2018.					X
31.1	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14 or 15d-14.					X
31.2	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14 or 15d-14.					X
32.1+	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Exchange Act Rules 13a-14(b) or 15d-14(b) and 18 U.S.C. Section 1350.					X
101.INS	XBRL Instance Document.					
101.SCH	XBRL Taxonomy Extension Schema Document.					
101.CAL	XBRL Taxonomy Extension Calculation Document.					
101.LAB	XBRL Taxonomy Extension Definition Linkbase Document.					
101.PRE	XBRL Taxonomy Extension Labels Linkbase Document.					
101.DEF	XBRL Taxonomy Extension Presentation Link Document.					

+ The certification furnished in Exhibit 32.1 hereto is deemed to be furnished with this Quarterly Report on Form 10-Q and will not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference

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.

Date: August 7, 2018

VOYAGER THERAPEUTICS, INC.

By: /s/ G. Andre Turenne
G. Andre Turenne
Chief Executive Officer, President, and Director
(Principal Executive Officer)

By: /s/ Allison Dorval
Allison Dorval
Vice President of Finance
(Principal Financial and Accounting Officer)

CONSULTING AGREEMENT

THIS AGREEMENT (together with the attached Accounting of Services Form, the "Agreement"), is entered into as of August 2, 2018 (the "Effective Date"), by and between Steven M. Paul, M.D., an individual residing at PH1A, Millennium Tower, 1 Franklin Street, Boston, MA 02110 (the "Consultant") and **Voyager Therapeutics, Inc.**, a Delaware corporation located at 75 Sidney Street, Cambridge, MA 02139 (hereinafter "Voyager").

WHEREAS, Voyager desires to retain the consulting and advisory services of Consultant with respect to certain activities as described in this Agreement, and Consultant is willing to so act.

NOW, THEREFORE, Consultant and Voyager agree as follows:

1. Description of Services. Voyager hereby retains Consultant as a consultant to Voyager and Consultant hereby agrees to use his best efforts to provide advice and assistance to Voyager in the area of Consultant's expertise from time to time as requested by Voyager (the "**Services**"). In particular, the Services shall include any specific activities described on the attached **Accounting of Services Form** attached hereto as Exhibit A, as well as a reasonable amount of additional advisory services to Voyager's personnel or designees by telephonic means, or in the form of reports and summaries, and such additional activities agreed to by the parties from time to time. Any changes to the Services (and any related compensation adjustments) must be agreed to in writing between Consultant and Voyager prior to implementation of the changes.
2. Term & Termination. The term of this Agreement shall be the twelve (12) month period commencing on August 2, 2018, unless earlier terminated in accordance with this Agreement or extended by mutual written agreement (the "**Term**"). This Agreement may be terminated prior to its expiration in the following manner: (i) by Voyager at any time immediately upon written notice to Consultant if Consultant has materially breached this Agreement, the Retirement Agreement dated June 28, 2018 between Consultant and the Company (the "**Retirement Agreement**"), or the Restrictive Covenants Agreement referenced in the Retirement Agreement; (ii) by Consultant at any time immediately upon written notice if Voyager has materially breached this Agreement or the Retirement Agreement; (iii) by either party at any time, for any reason or no reason, upon not less than forty-five (45) days prior written notice to the other party; (iv) at any time upon the mutual written consent of both parties; or (v) automatically upon the death, physical incapacitation or mental incompetence of Consultant. Any expiration or termination of this Agreement shall be without prejudice to any obligation of either party that has accrued prior to the effective date of expiration or termination. Upon expiration or termination of this Agreement, neither Consultant nor Voyager will have any further obligations under this Agreement, except that (a) Consultant will terminate all Services in progress in an orderly manner as soon as practicable and in accordance with a schedule agreed to by Voyager, unless Voyager specifies in the notice of termination that Services in progress should be completed; (b) Consultant will deliver to Voyager all Work Product (defined below) made through expiration or termination; (c) Voyager will pay Consultant any monies due and owing Consultant, up to the time of termination or expiration, for Services properly performed and all authorized expenses actually incurred; (d) Consultant will immediately return to Voyager all Voyager Property (defined below) and other Confidential Information (defined below) and copies thereof provided to Consultant under this Agreement; and (e) the terms, conditions and obligations under Sections 2 and 4 through 14 will survive expiration or termination of this Agreement.
3. Payment of Fees and Expenses. Voyager will pay Consultant for fees, expenses and pass-through costs in accordance with each Accounting of Services Form, including reasonable and necessary travel, lodging and meals in connection with the Services, subject to Voyager's travel policy. Unless otherwise agreed in an

Accounting of Services Form, the following shall apply:

- (a) Voyager will pay consultant monthly for the retainer amount
- (b) Consultant will invoice Voyager monthly for any additional fees, pre-approved expenses and pass-through costs relating to the Services. Invoices will reference the applicable PO number provided by Voyager, and are to be sent directly to Accounts Payable, Voyager Therapeutics, Inc., 75 Sidney St., Cambridge, MA 02139 or submitted via e-mail to: ap@vygr.com;
- (c) Voyager shall pay all undisputed amounts invoiced in accordance with the terms of this Section 3 within thirty (30) days of receipt of invoice.

Upon execution of this Agreement, Consultant shall submit a W-9/W-8BEN/W-8ECI (as applicable) to Voyager's Accounts Payable department at the address above. Invoices will not be paid without Voyager's receipt of Consultant's W-9/W-8BEN/W-8ECI information.

4. Compliance with Laws. Consultant represents and warrants that Consultant will render Services in compliance with all applicable laws, rules and regulations, including but not limited to the U.S. Food, Drug and Cosmetic Act, as amended from time to time, and the highest professional standards. Further, Consultant represents and warrants that he has not been, and is not under consideration to be (a) debarred from providing services pursuant to Section 306 of the United States Federal Food Drug and Cosmetic Act, 21 U.S.C. § 335a; (b) excluded, debarred or suspended from, or otherwise ineligible to participate in, any federal or state health care program or federal procurement or non-procurement programs (as that term is defined in 42 U.S.C. §1320a-7b(f)); (c) disqualified by any government or regulatory agencies from performing specific services, and is not subject to a pending disqualification proceeding; or (d) convicted of a criminal offense related to the provision of health care items or services, or under investigation or subject to any such action that is pending.
5. Compliance with Obligations to Third Parties. Consultant represents and warrants to Voyager that the terms of this Agreement and Consultant's performance of Services do not and will not conflict with any of Consultant's obligations to any third parties. Consultant represents that Consultant has not brought and will not bring with Consultant to Voyager or use in the performance of Services any equipment, funds, space, personnel, facilities, confidential information, trade secrets or other resources of any third party which are not generally available to the public, unless Consultant has obtained written authorization for their possession and use, nor will Consultant take any other action that would result in a third party, including without limitation, an employer of Consultant, asserting ownership of, or other rights in, any Work Product, unless agreed upon in writing in advance by Voyager. To the extent Consultant is subject to any policy of his employer that requires approval of agreements governing external consulting services, Consultant represents that such approval has been given and covenants that such approval will be obtained prior to entering into any amendment to this Agreement requiring such approval. Consultant will notify Voyager immediately of any breach of this Section 5.
6. Work Product. Consultant will promptly and fully disclose in confidence to Voyager all inventions, discoveries, improvements, ideas, concepts, designs, processes, formulations, products, computer programs, works of authorship, databases, mask works, trade secrets, know-how, information, data, documentation, reports, research, creations and other products arising from or made in the performance of (solely or jointly with others) the Services (whether or not patentable or subject to copyright or trade secret protection) (collectively, the "**Work Product**"). Consultant assigns and agrees to assign to Voyager all rights in the United States and throughout the world to Work Product. Consultant will keep and maintain adequate and current written records of all Work Product, and such records will be available to and remain the sole property of Voyager at all times. For purposes of the copyright laws of the United States, Work Product will constitute "works made for hire," except to the extent such Work Product cannot by law be "works

made for hire”. Consultant represents and warrants that Consultant has and will have the right to transfer and assign to Voyager ownership of all Work Product. Consultant will execute all documents, and take any and all actions needed, all without further consideration, in order to confirm Voyager’s rights as outlined above. In the event that Consultant should fail or refuse to execute such documents within a reasonable time, Consultant appoints Voyager as attorney to execute and deliver any such documents on Consultant’s behalf.

7. Confidentiality & Non-Use. During the Term and thereafter, except as otherwise permitted as set forth below, Consultant agrees to (a) hold the Confidential Information in confidence; (b) exercise reasonable precautions to physically protect the integrity and confidentiality of the Confidential Information; (c) not disclose any Confidential Information to any third party without the prior written consent of Voyager; (d) not use the Confidential Information for any purpose except as may be necessary in the ordinary course of performing Services without the prior written consent of Voyager; (e) treat Confidential Information with no less than a reasonable degree of care; and (f) reproduce Confidential Information solely to the extent necessary to provide the Services, with all such reproductions being considered Confidential Information.

Voyager’s “**Confidential Information**” means (i) all Work Product; (ii) all information contained in or comprised of Voyager Property (defined in Section 8); and (iii) all confidential and proprietary data, trade secrets, business plans, and other information of a confidential or proprietary nature in written, electronic or other media, belonging to Voyager or its subsidiaries or third parties with whom Voyager may have business dealings, disclosed or otherwise made available to Consultant by Voyager or on behalf of Voyager in connection with this Agreement and/or Consultant’s services hereunder. Consultant’s obligations of non-disclosure and non-use under this Agreement will not apply to any portion of Confidential Information that Consultant establishes by competent proof: (a) was in the public domain at the time of disclosure through no wrongful act on the part of Consultant; (b) after disclosure, becomes part of the public domain by publication or otherwise, except by a wrongful act on the part of Consultant; ; (c) becomes known to Consultant on a non-confidential basis through disclosure by sources other than Voyager having the legal right to disclose such Confidential Information; or (d) is independently developed by Consultant without reference to or reliance upon Confidential Information.

Nothing in this Agreement prohibits Consultant from communicating with government agencies about possible violations of federal, state, or local laws or otherwise providing information to government agencies, filing a complaint with government agencies, or participating in government agency investigations or proceedings. Consultant is not required to notify the Company of any such communications; provided, however, that nothing herein authorizes the disclosure of information Consultant obtained through a communication that was subject to the attorney-client privilege. Further, notwithstanding Consultant’s confidentiality and nondisclosure obligations, Consultant is hereby advised as follows pursuant to the Defend Trade Secrets Act: “An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order.”

8. Voyager Property. All documents, data, records, apparatus, equipment and other physical property furnished or made available by or on behalf of Voyager to Consultant in connection with this Agreement (“**Voyager Property**”) shall be and remain the sole property of Voyager and shall be returned promptly to

Voyager if requested. In any event, Consultant shall return and deliver all Voyager Property, including any copies thereof, upon termination or expiration of this Agreement, irrespective of the reason for such termination. Consultant will use Voyager Property only as necessary to perform the Services and will not transfer or make available to any third party the Voyager Property without the express prior written consent of Voyager. Consultant recognizes that Voyager's facilities are private and Consultant will abide by Voyager's security requirements and conditions for access and usage and agrees that only those subjects, areas and programs designated by Voyager as necessary to fulfill Voyager's requirements will be accessed and/or perused Consultant. In no event will any Confidential Information, programs or other information be copied or removed without Voyager's express written approval.

9. Publication; Publicity. Work Product may not be published or referred to, in whole or in part, by Consultant without the prior express written consent of Voyager. Consultant shall not use the name, logo, trade name, service mark, or trademark, or any simulation, abbreviation, or adaptation of same, or the name of Voyager or its subsidiaries for publicity, promotion, or similar non-regulatory uses without Voyager's prior written consent.
10. Independent Contractor Relationship. Nothing contained in this Agreement shall be deemed to constitute Consultant an employee of Voyager, it being the intent of the parties to establish an independent contractor relationship, nor shall Consultant have authority to bind Voyager in any manner whatsoever by reason of this Agreement. Consultant shall at all times while on Voyager premises observe all security and safety policies of Voyager. Consultant is excluded from participating in any fringe benefit plans or programs as a result of the performance of the Services, without regard to Consultant's independent contractor status, including, but not limited to, health, sickness, accident or dental coverage, life insurance, disability benefits, accidental death and dismemberment coverage, unemployment insurance coverage, workers' compensation coverage, 401(k) benefit(s), and any other benefits provided by Voyager to its employees. Consultant agrees, as an independent contractor, that Consultant is not entitled to unemployment benefits in the event this Agreement terminates, or workers' compensation benefits in the event that Consultant is injured in any manner or becomes ill while performing the Services under this Agreement. Because Consultant is an independent contractor, Voyager will not make any withholdings, deductions, or contributions (e.g., social security, unemployment insurance, disability insurance) from Consultant's fees, and will report Consultant's fees and other payments to Consultant on a 1099 form. Consultant shall bear sole responsibility for paying and reporting its own applicable federal and state income taxes, social security taxes, unemployment insurance, workers' compensation, and health or disability insurance, retirement benefits, and other welfare or pension benefits, if any, and shall indemnify and hold Voyager harmless from and against any liability with respect thereto.
11. Notices. All notices required or permitted under this Agreement must be in writing. Any notice given under this Agreement shall be deemed delivered when delivered by hand, by certified mail, by air courier or via facsimile to the parties at their respective addresses set forth above or at such other address as either party may provide to the other in writing from time to time. Notices will be effective upon receipt or at a later date stated in the notice.
12. Assignment. The rights and obligations of the parties hereunder shall inure to the benefit of, and shall be binding upon their respective successors and assigns. This Agreement may not be assigned by Consultant, and Consultant's obligations under this Agreement may not be subcontracted or delegated by Consultant, without the prior written consent of Voyager. For clarity, this Agreement may be assigned by Voyager with prompt notice of such assignment to Consultant.
13. Specific Enforcement. Consultant acknowledges that Voyager will have no adequate remedy at law in the event Consultant breaches the terms of Sections 4 through 9. In addition to any other rights it may have,

Voyager shall have the right to obtain in any court of competent jurisdiction injunctive or other relief to restrain any breach or threatened breach of this Agreement.

14. Prior Agreements; Governing Law; Severability; Amendment. This Agreement embodies the entire understanding between the parties with respect to the subject matter of this Agreement and supersedes any prior or contemporaneous agreements with respect to the subject matter of this Agreement; provided, however, for the avoidance of doubt, that Consultant's obligations pursuant to Sections 6, 7 and 8 hereunder are in addition to any and all similar ongoing obligations that Consultant has to Voyager pursuant to the Retirement Agreement and/or the Restrictive Covenants Agreement referenced therein. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts, without regard to any choice of law principle that would dictate the application of the law of another jurisdiction, and Consultant submits to the jurisdiction and agrees to the proper venue of all state and federal courts located within the Commonwealth of Massachusetts. Each provision in this Agreement is independent and severable from the others, and no provision will be rendered unenforceable because any other provision is found by a proper authority to be invalid or unenforceable in whole or in part. If any provision of this Agreement is found by such an authority to be invalid or unenforceable in whole or in part, such provision shall be changed and interpreted so as to best accomplish the objectives of such unenforceable or invalid provision and the intent of the parties, within the limits of applicable law. This Agreement may be executed in one or more counterparts, each of which will be deemed an original, and all of which together will be deemed to be one and the same instrument. A facsimile or electronic copy of this Agreement, including the signature pages, will be deemed an original. This Agreement may not be amended, and its terms may not be waived, except pursuant to a written amendment or waiver signed by both parties.
15. Insurance. Consultant shall maintain such insurance as shall be reasonably necessary to insure itself against any claim or claims for damages arising out of the Services or this Agreement. Consultant shall provide evidence of such coverage to the Voyager upon request.
16. Certain Other Conflicts of Interest; Trading in Voyager Securities.
- (a) Consultant represents that, except as disclosed in writing to Voyager, Consultant: (i) does not own directly or indirectly five percent (5%) or more of the stock or other equity securities of any entity which is a present or prospective competitor, customer or supplier of Voyager; (ii) is not aware of any legal proceedings pending or threatened against Consultant, or any reasonable basis for such proceedings, which (1) would conflict with Consultant's obligations hereunder or question the validity of this Agreement; or (2) may materially or adversely affect the business or prospects of Voyager; and (iii) is not aware of any fact concerning Consultant (either professionally or personally) which may materially or adversely affect the business or prospects of Voyager.
- (b) Consultant is aware that the United States and other applicable securities laws prohibit any person who has material, non-public information about a company from purchasing or selling securities of such company or from communicating such information to any other person under circumstances in which it is reasonably foreseeable that such person is likely to purchase or sell such securities. Consultant may gain access to information in connection with the provision of Services that could potentially subject Consultant to insider trading liability (as defined under the US federal securities laws and regulations adopted by the United States Securities and Exchange Commission) in connection with trading in Voyager securities. Consultant shall comply with all relevant laws respecting any trading in Voyager securities.

IN WITNESS WHEREOF, the parties hereto have entered into this Agreement as of the Effective Date.

CONSULTANT

VOYAGER THERAPEUTICS, INC.

By: _____

By: _____

Name: _____

Name: _____

Tax ID#: _____

Title: _____

EXHIBIT A
ACCOUNTING OF SERVICES FORM

**Consulting Agreement Between Voyager Therapeutics, Inc. (“Voyager”) and
Steven M. Paul M.D. (“Consultant”) Dated August 2, 2018**

1. Services:

Consultant will provide the following Services to Voyager:

Consultant will act as a Senior Advisor to Voyager, and will provide consulting and advisory services including scientific guidance to the AbbVie collaboration team, strategic guidance to Voyager’s R&D programs, and executive consultation on business development efforts.

Consultant will provide Services on a schedule and at a location or locations mutually agreed between Consultant and Andre Turenne, President & Chief Executive Officer. The current expectation is that Consultant will generally be onsite in Voyager’s Cambridge, MA offices once per week. In addition, Consultant will be available for a reasonable number of telephone and/or written consultations.

2. Compensation:

Fees: Voyager will pay Consultant consulting fees of \$16,700 per month, not to exceed \$200,500 during the initial Term, without Voyager’s express written consent.

Expenses: Voyager will reimburse Consultant for any pre-approved expenses actually incurred by Consultant in connection with the provision of Services. Requests for reimbursement will be in a form reasonably acceptable to Voyager, will include supporting documentation and will accompany Consultant’s invoices.

Support: Voyager will provide Consultant with administrative support, as may be reasonably required to facilitate provision of the Services.

Invoicing: No invoice will be required for the retainer, which will be paid monthly. No later than the last day of each calendar month, Consultant will invoice Voyager for related expenses incurred during the preceding month. Invoices should reference this Agreement and should be submitted to Voyager by email to: ap@vygr.com. Invoices will contain such detail as Voyager may reasonably require and will be payable in U.S. Dollars. Undisputed payments will be made by Voyager within thirty (30) days after Voyager’s receipt of Consultant’s invoice, request for reimbursement and all supporting documentation.

3. Period of Performance:

Services are anticipated to commence on August 2, 2018 and be complete within twelve months of commencement.

Certification

I, G. Andre Turenne, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the period ended June 30, 2018 of Voyager 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(s) 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: August 7, 2018

/s/ G. Andre Turenne

G. Andre Turenne
Chief Executive Officer, President, and Director
(Principal Executive Officer)

Certification

I, Allison Dorval, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the period ended June 30, 2018 of Voyager 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(s) 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: August 7, 2018

/s/ Allison Dorval

Allison Dorval
Vice President of Finance
(Principal Financial and Accounting Officer)

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

In connection with the Quarterly Report on Form 10-Q of Voyager Therapeutics, Inc. (the "Company") for the period ended June 30, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 that to his or her knowledge:

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

Date: August 7, 2018

/s/ G. Andre Turenne

G. Andre Turenne

*Chief Executive Officer, President, and Director
(Principal Executive Officer)*

Date: August 7, 2018

/s/ Allison Dorval

Allison Dorval

Vice President of Finance

(Principal Financial and Accounting Officer)
