Table of Contents

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, 2020.

☐ **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)	**46-3003182** (I.R.S. Employer Identification No.)
75 Sidney Street, Cambridge, Massachusetts (Address of principal executive offices)	**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)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value	VYGR	Nasdaq Global Select Market

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

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

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

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

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

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

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of August 5, 2020 was 37,431,028.

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 (which our partner Neurocrine Biosciences, Inc., or Neurocrine, refers to as NBIb-1817) as a treatment for Parkinson’s disease through the Phase 1b clinical trial, the separate Phase 1 clinical trial, and the RESTORE-1 Phase 2 clinical trial, and our preclinical development efforts and studies;
- formulation changes to our product candidates that 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-HTT01 for the treatment of Huntington’s disease, VY-SOD102 for the treatment of a monogenic form of amyotrophic lateral sclerosis, 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, maintain and enforce 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 AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company, or collectively AbbVie, and Neurocrine;
- 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 the Phase 1b clinical trial and the separate Phase 1 clinical trial focused on posterior trajectory in future clinical trials, including the RESTORE-1 Phase 2 trial;
- our ability to enter into future collaborations, strategic alliances, or licensing arrangements; and
- the potential impact of the COVID-19 pandemic on our clinical trials and other business operations.

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 3, 2020 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

TABLE OF CONTENTS

PART I. FINANCIAL INFORMATION

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

	June 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 144,321	$ 86,042
Marketable securities, current	85,349	195,491
Related party collaboration receivable	12,686	18,496
Prepaid expenses and other current assets	4,301	4,630
Total current assets	246,657	304,659
Property and equipment, net	20,205	17,986
Deposits and other non-current assets	2,183	1,723
Marketable securities, non-current	1,422	1,920
Operating lease, right-of-use asset	26,988	28,472
Total assets	$ 297,455	$ 354,760
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,045	$ 4,070
Accrued expenses	18,154	21,516
Other current liabilities	3,421	3,193
Deferred revenue, current	43,911	47,233
Total current liabilities	67,531	76,012
Deferred revenue, non-current	122,856	147,260
Other non-current liabilities	30,184	31,976
Total liabilities	220,571	255,248
Commitments and contingencies (see note 6 & 8)		
Stockholders' equity:		
Preferred stock $0.001 par value: 5,000,000 shares authorized at June 30, 2020 and December 31, 2019; no shares issued and outstanding at June 30, 2020 and December 31, 2019	—	—
Common stock, $0.001 par value: 120,000,000 shares authorized at June 30, 2020 and December 31, 2019; 37,203,627 and 36,865,116 shares issued and outstanding at June 30, 2020 and December 31, 2019, respectively	37	37
Additional paid-in capital	422,294	412,227
Accumulated other comprehensive income (loss)	145	(104)
Accumulated deficit	(345,592)	(312,648)
Total stockholders' equity	76,884	99,512
Total liabilities and stockholders' equity	$ 297,455	$ 354,760

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 June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Collaboration revenue	$ 28,681	$ 46,087	$ 46,748	$ 51,284
Operating expenses:				
Research and development	29,423	28,576	61,718	53,407
General and administrative	8,239	8,322	18,444	17,981
Total operating expenses	37,662	36,898	80,162	71,388
Operating (loss) income	(8,981)	9,189	(33,414)	(20,104)
Other income, net:				
Interest income	346	2,097	1,324	3,242
Other (expense) income	(46)	(133)	(854)	845
Total other income, net	300	1,964	470	4,087
Net (loss) income	$ (8,681)	$ 11,153	$ (32,944)	$ (16,017)
Other comprehensive (loss) income				
Net unrealized (loss) gain on available-for-sale securities	(276)	176	249	234
Total other comprehensive (loss) income	(276)	176	249	234
Comprehensive (loss) income	$ (8,957)	$ 11,329	$ (32,695)	$ (15,783)
Net (loss) income per share, basic	$ (0.23)	$ 0.30	$ (0.89)	$ (0.46)
Net (loss) income per share, diluted	$ (0.23)	$ 0.29	$ (0.89)	$ (0.46)
Weighted-average common shares outstanding, basic	37,029,524	36,610,918	36,996,390	34,990,989
Weighted-average common shares outstanding, diluted	37,029,524	37,941,257	36,996,390	34,990,989

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

Voyager Therapeutics, Inc.
Condensed Consolidated Statements of Stockholders' Equity
(amounts in thousands, except share data)
(unaudited)

	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Stockholders' Equity (Deficit)
Balance at December 31, 2018	32,364,895	$ 32	$ 315,598	$ (133)	$ (269,051)	$ 46,446
Exercises of vested stock options	31,360	1	283	—	—	284
Issuance of common stock in connection with the Neurocrine Collaboration Agreement	4,179,728	4	77,613	—	—	77,617
Stock-based compensation expense	—	—	3,459	—	—	3,459
Unrealized gain on available-for-sale securities, net of tax	—	—	—	58	—	58
Net loss	—	—	—	—	(27,170)	(27,170)
Balance at March 31, 2019	36,575,983	$ 37	$ 396,953	$ (75)	$ (296,221)	$ 100,694
Exercises of vested stock options	57,461	—	714	—	—	714
Issuance of common stock under ESPP	44,164	—	471	—	—	471
Stock-based compensation expense	—	—	5,196	—	—	5,196
Unrealized gain on available-for-sale securities, net of tax	—	—	—	176	—	176
Net income	—	—	—	—	11,153	11,153
Balance at June 30, 2019	36,677,608	$ 37	$ 403,334	$ 101	$ (285,068)	$ 118,404
Balance at December 31, 2019	36,865,116	$ 37	$ 412,227	$ (104)	$ (312,648)	$ 99,512
Exercises of vested stock options	3,035	—	34	—	—	34
Vesting of restricted stock units	108,600	—	—	—	—	—
Stock-based compensation expense	—	—	3,949	—	—	3,949
Unrealized gain on available-for-sale securities, net of tax	—	—	—	525	—	525
Net loss	—	—	—	—	(24,263)	(24,263)
Balance at March 31, 2020	36,976,751	$ 37	$ 416,210	$ 421	$ (336,911)	$ 79,757
Exercises of vested stock options	160,478	—	1,651	—	—	1,651
Vesting of restricted stock units	21,403	—	—	—	—	—
Issuance of common stock under ESPP	44,995	—	638	—	—	638
Stock-based compensation expense	—	—	3,795	—	—	3,795
Unrealized loss on available-for-sale securities, net of tax	—	—	—	(276)	—	(276)
Net loss	—	—	—	—	(8,681)	(8,681)
Balance at June 30, 2020	37,203,627	$ 37	$ 422,294	$ 145	$ (345,592)	$ 76,884

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,	
	2020	**2019**
Cash flow from operating activities		
Net loss	$ (32,944)	$ (16,017)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Stock-based compensation expense	7,900	8,771
Depreciation	1,768	1,292
Amortization of premiums and discounts on marketable securities	(122)	(1,844)
In-kind research and development expenses	—	616
Other non-cash items	854	(832)
Changes in operating assets and liabilities:		
Related party collaboration receivable	5,810	(10,063)
Prepaid expenses and other current assets	995	2,966
Operating lease, right-of-use asset	1,484	1,382
Other non-current assets	139	(674)
Accounts payable	(2,025)	1,192
Accrued expenses	(4,568)	1,977
Operating lease liabilities	(1,564)	(1,226)
Deferred revenue	(27,726)	106,065
Net cash (used in) provided by operating activities	(49,999)	93,605
Cash flow from investing activities		
Purchases of property and equipment	(3,389)	(3,168)
Loss from sale of equipment	31	171
Purchases of marketable securities	(14,987)	(314,352)
Proceeds from maturities of marketable securities	125,500	177,800
Net cash provided by (used in) investing activities	107,155	(139,549)
Cash flow from financing activities		
Proceeds from the exercise of stock options	1,685	998
Proceeds from the issuance of common stock in connection with the Neurocrine Collaboration Agreement, net	—	77,617
Proceeds from the purchase of common stock under ESPP	482	355
Net cash provided by financing activities	2,167	78,970
Net increase in cash, cash equivalents, and restricted cash	59,323	33,026
Cash, cash equivalents, and restricted cash beginning of period	86,777	47,594
Cash, cash equivalents, and restricted cash end of period	$ 146,100	$ 80,620
Supplemental disclosure of cash and non-cash activities		
Capital expenditures incurred but not yet paid	$ 1,603	$ 17

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. In addition to the Company's capsid optimization efforts, it leverages novel delivery paradigms, established routes of administration, and advances in dosing techniques to optimize delivery of its AAV gene therapies to target tissues, regions and cell types that are critical to the disease of interest. The Company believes it can achieve this directly, with targeted infusions to discrete regions of the brain, the spinal cord, or systemically, in conjunction with its novel capsids.

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 Corporation (the "Sanofi Genzyme Collaboration"), its collaboration with AbbVie Biotechnology Ltd (the "AbbVie Tau Collaboration"), its collaboration with Neurocrine Biosciences, Inc. (the "Neurocrine Collaboration"), and its collaboration with AbbVie Ireland Unlimited Company (the "AbbVie Alpha-Synuclein 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 industries, including but not limited to, the need to obtain sufficient capital to continue to fund its operations, 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 information and technology, protection against data breaches and other cybersecurity threats, 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, 2020, the Company had an accumulated deficit of $345.6 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 its collaborations with Sanofi Genzyme Corporation ("Sanofi Genzyme"), AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company (collectively, "AbbVie"), and Neurocrine Biosciences, Inc. ("Neurocrine").

Through June 30, 2020, the Company has raised approximately $640.0 million of proceeds from sales of convertible preferred stock and common stock, including its initial public offering and follow-on public offering, and proceeds from collaboration agreements. As of June 30, 2020, the Company had cash, cash equivalents, and marketable debt securities of $229.7 million. Based upon its current operating plan, the Company expects that its existing cash, cash equivalents, and marketable debt securities, as well as ongoing reimbursement amounts expected from development

costs related to its collaboration and license agreement with Neurocrine, or the Neurocrine Collaboration Agreement, will enable the Company to meet its planned operating expenses and capital expenditure requirements into mid-2022.

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 collaboration 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.

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, 2019 as filed with the Securities and Exchange Commission ("SEC") on March 3, 2020. 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"). See "*Recently Adopted Accounting Pronouncements*" below for discussion of the Company's adoption of new guidance effective January 1, 2020. All amounts and disclosures set forth in this Quarterly Report on Form 10-Q reflect adoption of these changes.

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 and Basis of Presentation, within the "Notes to Consolidated Financial Statements" accompanying the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019. Intercompany accounts and transactions have been eliminated.

Use of estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated 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, and income taxes. 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. Certain reclassifications have been made to prior periods to conform to current period presentation.

Summary of Significant Accounting Policies

There have been no changes in the Company's significant accounting policies as described in, *Summary of Significant Accounting Policies* to the consolidated financial statements in its Annual Report on Form 10-K for the year ended December 31, 2019.

Recently Adopted Accounting Pronouncements

In 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), which amends the impairment model by requiring entities to use a forward-looking approach based on expected losses to estimate credit losses on certain types of financial

instruments, including trade receivables and available-for-sale debt securities. The Company adopted the standard on January 1, 2020. Based on the composition of the Company's investment portfolio, current market conditions, and historical credit loss activity, the adoption of this standard did not have a material impact on the Company's consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"). This standard eliminates, adds and modifies certain disclosure requirements for fair value measurements as part of its disclosure framework project. The Company adopted the standard on the required effective date of January 1, 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial statements and related disclosures.

3. Fair value measurements

Assets and liabilities measured at fair value on a recurring basis as of June 30, 2020 and December 31, 2019 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)
June 30, 2020		*(in thousands)*		
Money market funds included in cash and cash equivalents	$ 137,755	$ 137,755	$ —	$ —
Marketable securities:				
U.S. Treasury notes	85,349	85,349	—	—
Equity securities	1,422	1,422	—	—
Total marketable securities	$ 86,771	$ 86,771	$ —	$ —
Warrants to purchase equity securities	198	—	198	—
Total	$ 224,724	$ 224,526	$ 198	$ —
December 31, 2019				
Money market funds included in cash and cash equivalents	$ 78,303	$ 78,303	$ —	$ —
Marketable securities:				
U.S. Treasury notes	195,491	195,491	—	—
Equity securities	1,920	1,920	—	—
Total marketable securities	$ 197,411	$ 197,411	$ —	$ —
Warrants to purchase equity securities	554	—	554	—
Total	$ 276,268	$ 275,714	$ 554	$ —

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 as of June 30, 2020 and December 31, 2019 are as follows:

	As of June 30, 2020	As of December 31, 2019
Risk-free interest rate	0.2 %	1.6 %
Expected dividend yield	— %	— %
Expected term (in years)	1.2	1.7
Expected volatility	69.1 %	71.6 %

The expected volatility is based on the historic volatility for the equity securities 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, restricted cash, and available-for-sale marketable securities

Cash, cash equivalents, and marketable securities included the following at June 30, 2020 and December 31, 2019:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
		(in thousands)		
As of June 30, 2020				
Money market funds included in cash and cash equivalents	$ 137,755	$ —	$ —	$ 137,755
Marketable securities:				
U.S. Treasury notes	85,075	273	—	85,349
Equity securities	1,220	202	—	1,422
Total marketable securities	$ 86,295	$ 475	$ —	$ 86,771
Total money market funds and marketable securities	$ 224,050	$ 475	$ —	$ 224,526
As of December 31, 2019				
Money market funds included in cash and cash equivalents	$ 78,303	$ —	$ —	$ 78,303
Marketable securities:				
U.S. Treasury notes	195,467	52	28	195,491
Equity securities	1,220	700	—	1,920
Total marketable securities	$ 196,687	$ 752	$ 28	$ 197,411
Total money market funds and marketable securities	$ 274,990	$ 752	$ 28	$ 275,714

All of the Company's marketable debt securities at June 30, 2020, have a contractual maturity of one year or less.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash within the condensed consolidated balance sheets that sum to the total of the same such amounts shown in the condensed consolidated statements of cash flows:

	As of June 30, 2020	As of December 31, 2019
	(in thousands)	
Cash and cash equivalents	$ 144,321	$ 86,042
Restricted cash included in deposits and other non-current assets	1,779	735
Total cash, cash equivalents, and restricted cash	$ 146,100	$ 86,777

5. Accrued expenses

Accrued expenses as of June 30, 2020 and December 31, 2019 consist of the following:

	As of June 30, 2020	As of December 31, 2019
	(in thousands)	
Research and development costs	$ 10,462	$ 13,248
Employee compensation costs	4,492	5,733
Accrued goods and services	1,764	1,386
Professional services	1,333	897
Other	103	252
Total	$ 18,154	$ 21,516

6. Lease obligation

Operating Leases

As of June 30, 2020, the Company has leases for office and lab space at 75 and 64 Sidney Street in Cambridge, Massachusetts through November 30, 2026.

In March 2020, the Company entered into an agreement to lease an additional facility at 75 Hayden Avenue in Lexington, Massachusetts through October 29, 2030. The facility includes laboratory and office space. The Company currently expects the facility to be ready for occupancy in late 2020. As of June 30, 2020, the Company did not have control of the space and therefore, did not record a right-of-use asset and corresponding lease liability. The expected contractual obligation under this lease is approximately $25.6 million, to be paid over the ten-year term of the lease. These payments are not included in the detailed table below.

The Company has received leasehold improvement incentives from the landlord totaling $1.3 million and $3.5 million for 75 Sidney Street and 64 Sidney Street, respectively. The Company recorded these incentives as a component of its right-of-use asset and is amortizing these incentives as a reduction of rent expense over the life of the leases. The leasehold improvements have been capitalized as fixed assets. The Company is entitled to receive approximately $0.1 million of leasehold improvements at 75 Sidney Street. The Company is also entitled to receive approximately $6.1 million of leasehold improvements for the space at 75 Hayden Avenue.

The Company's lease agreements require the Company to maintain a cash deposit or irrevocable letter of credit in the aggregate amount of $1.8 million payable to the landlords as security for the performance of its obligations under the leases. These amounts are recorded as restricted cash and included in deposits and other non-current assets in the accompanying condensed consolidated balance sheets.

The following table summarizes the Company's significant contractual obligations under operating leases as of payment due date by period at June 30, 2020:

	Total Minimum Lease Payments
	(in thousands)
2020 (remainder of year)	$ 2,980
2021	6,138
2022	6,323
2023	6,512
2024	6,707
2025+	14,190
Total future minimum lease payments	$ 42,850
Less: imputed interest	(10,246)
Total lease liability	$ 32,604
Reported as:	
Other current liabilities	$ 3,421
Other non-current liabilities	29,183
Total lease liability	$ 32,604

During the three and six months ended June 30, 2020, the Company incurred lease expense of $1.7 million and $3.4 million, respectively, for operating leases. As of June 30, 2020, the weighted average remaining lease term was 6.4 years and the weighted average incremental borrowing rate used to determine the operating lease liability was 8.5%.

7. Other liabilities

As of June 30, 2020 and December 31, 2019, other current and non-current liabilities consisted of the following:

	As of June 30, 2020	As of December 31, 2019
	(in thousands)	
Other current liabilities		
Lease liability	3,421	3,193
Total other current liabilities	$ 3,421	$ 3,193
Other non-current liabilities		
Lease liability	$ 29,183	$ 30,975
Other	1,001	1,001
Total other non-current liabilities	$ 30,184	$ 31,976

8. Commitments and contingencies

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 to the Company. In addition, contemporaneous with entering into the Sanofi Genzyme Collaboration Agreement, Sanofi Genzyme entered into a Series B Stock Purchase Agreement with the Company, under which Sanofi Genzyme purchased 10,000,000 shares of the Company's 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 (NBIb-1817) for Parkinson's disease (the "VY-AADC Program"), VY-FXN01 for Friedreich's ataxia (the "FA Program"), a future program to be designated by Sanofi Genzyme (the "Future Program"), and VY-HTT01 for Huntington's disease (the "Huntington's Program"), with an incremental option to co-commercialize VY-HTT01 in the United States and (ii) worldwide rights to VY-SMN101 (the "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.

The Company was solely responsible for all costs incurred in connection with the development of the Split Territory Programs and the Spinal Muscular Atrophy Program 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 would provide "in-kind" services valued at up to $5.0 million and (ii) Sanofi Genzyme would be responsible for the costs and expenses of activities under the Huntington's Program development plan to the extent such activities were covered by financial support Sanofi Genzyme is entitled to receive from a patient advocacy group.

Termination of Agreement

On June 14, 2019 (the "Termination Date"), the Company and Sanofi Genzyme executed a termination agreement to terminate the Sanofi Genzyme Collaboration Agreement (the "Sanofi Genzyme Termination Agreement"). Under the terms of the Sanofi Genzyme Termination Agreement, Sanofi Genzyme relinquished its rights to the exclusive license options to the Huntington's Program, the FA Program and the Future Program. The Company has been relieved of its obligations to perform the research and development services under those programs through completion of the respective POP Studies. As a result, the Company gained worldwide rights to the Huntington's Program and ex-U.S. rights to the FA Program. The ex-U.S. rights to the FA Program have been, in turn, transferred from the Company to Neurocrine Biosciences pursuant to the collaboration and option agreement with Neurocrine Biosciences. Additionally, the Company and Sanofi Genzyme entered into an Amended and Restated Option and License Agreement related to AAV capsids (the "Amended Capsid Agreement"). Under the Amended Capsid Agreement, Sanofi Genzyme has obtained exclusive option rights to exclusively license up to two select novel AAV capsids owned or controlled by the Company for exclusive use for up to two non-central nervous system ("non-CNS") indications.

Sanofi Genzyme has granted the Company exclusive, irrevocable, perpetual, royalty-free, fully-paid sublicensable (through multiple tiers), non-transferable, worldwide licenses in Sanofi Genzyme's interests in the collaboration technology generated under or used in the Huntington's Program and the FA Program with respect to those programs pursuant to the Sanofi Genzyme Collaboration Agreement. In addition, Sanofi Genzyme has granted the Company non-exclusive, irrevocable, perpetual, royalty-free, fully-paid, sublicensable (through multiple tiers), non-transferable, worldwide licenses to the Sanofi Genzyme technology that was contributed to the Sanofi Genzyme Collaboration Agreement and was used in the development or manufacture of product candidates prior to the termination date.

Under the Sanofi Genzyme Termination Agreement, the Company made a $10.0 million upfront payment to Sanofi Genzyme and has agreed to make a $10.0 million milestone payment to Sanofi Genzyme within fifteen days of the filing of an investigational new drug ("IND") application for a product candidate incorporating certain intellectual property rights developed under or substantially related to the Huntington's Program (a "Post-Termination HD Product"). The Company has agreed to pay Sanofi Genzyme (i) 50% of any income received from sublicensing arrangements related to Post-Termination HD Products in excess of specified thresholds and entered into prior to (a) the filing of an IND application for a Post-Termination HD Product or (b) the dosing of the first patient in a clinical trial for a Post-Termination HD Product in the United States or certain European countries, respectively and (ii) a low-double digit percentage of any income received from sublicensing arrangements outside the United States related to products incorporating intellectual property rights developed under, or substantially related to, the FA Program (collectively, "Post-Termination FA Products") that are in excess of a specified threshold and entered into prior to the dosing of the first patient in a clinical trial for a Post-Termination FA Product in the United States or certain European countries, in each case, subject to certain limitations. The Company has also agreed to pay low-single digit royalties on net sales of Post-Termination HD Products. Under the Sanofi Genzyme Collaboration Agreement, the Company had rights to certain in-kind services. As of the effective date of the Sanofi Genzyme Termination Agreement, the Company waived its right to approximately $0.4 million in unused in-kind services, relinquished its rights to the Spinal Muscular Atrophy Program, and no longer has the right to receive any option payments, regulatory or commercial milestone payments or royalties from Sanofi Genzyme under the Sanofi Genzyme Collaboration Agreement.

The Company has granted Sanofi Genzyme an exclusive royalty-free, fully-paid, sublicensable (through multiple tiers), non-transferable, worldwide license under the Company's interest in the collaboration technology generated under or used in the Spinal Muscular Atrophy Program pursuant to the Sanofi Genzyme Collaboration Agreement to manufacture, develop, and commercialize any Spinal Muscular Atrophy product. Under the Amended Capsid Agreement, the Company has granted Sanofi Genzyme an exclusive option to evaluate up to four capsids for no consideration. During the capsid evaluation period, the Company has granted Sanofi Genzyme a non-exclusive license to the capsid intellectual property to conduct evaluation studies. In addition, Sanofi Genzyme is able to evaluate up to two additional capsids for a low six-figure payment per additional capsid. The Company is not obligated to perform any additional research on the capsids. Sanofi Genzyme shall have the right to obtain an exclusive license for up to two capsids, each in a specified non-CNS indication. At its discretion, Sanofi Genzyme may exercise both its options for the same capsid for different specified non-CNS indications. Upon its exercise of each option, Sanofi Genzyme has agreed

to pay the Company a $1.0 million option exercise fee. Under the Amended Capsid Agreement, the Company is also entitled to receive potential development and regulatory milestone payments upon the achievement of certain milestone events for products containing licensed capsids ("Sanofi Licensed Products") of up to an aggregate of $15.0 million per Sanofi Licensed Product. In addition, for each specified indication, Sanofi Genzyme has agreed to pay to the Company a one-time sales milestone payment of $20.0 million, if aggregate worldwide net sales for all Sanofi Licensed Products for such specified indication surpass a specified amount, and low-to-mid single-digit tiered royalty payments on worldwide net sales of Sanofi Licensed Products, on a Sanofi Licensed Product-by-Sanofi Licensed Product basis.

Accounting Analysis

The Sanofi Genzyme Termination Agreement modifies both the pricing and scope of the Sanofi Genzyme Collaboration Agreement. As the modification does not add distinct goods or services to the Sanofi Genzyme Collaboration Agreement, the agreement is considered a modification of the original contract.

The Sanofi Genzyme Termination Agreement includes the following performance obligations: (i) worldwide license to collaboration technology and Sanofi Genzyme technology for the development, manufacturing and commercialization of the Huntington's Program and (ii) worldwide license to collaboration technology and Sanofi Genzyme technology for the development, manufacturing and commercialization for the FA Program. Such performance obligations were satisfied upon the Termination Date as control had transferred upon execution of the Sanofi Genzyme Termination Agreement. Therefore, the remainder of the transaction price under the Sanofi Genzyme Collaboration Agreement, which had not yet been recognized, was recognized as revenue upon the Termination Date.

The Company has recognized $28.7 million of revenue upon the Termination Date. This amount consists of $48.7 million of deferred revenue related to the original agreement as of the Termination Date, offset by (x) $10.0 million related to the fee paid by the Company to Sanofi Genzyme on the Termination Date, and (y) $10.0 million related to the milestone payment which the Company expects to pay to Sanofi Genzyme upon the potential filing of an IND application for a product candidate in connection with the Huntington's Program. The Company recently completed IND-enabling preclinical studies and is in the process of finalizing an IND application for submission to the U.S. Food and Drug Administration ("FDA") for VY-HTT01 for the treatment of Huntington's disease, which it expects to file during the second half of 2020. Following clearance of the IND by the FDA, the Company expects to begin the first-in-human clinical trial of VY-HTT01 in Huntington's disease patients.

The Company has constrained $10.0 million of the remaining deferred revenue balance at the Termination Date as it expects to pay the milestone payment related to the potential filing of an IND for a product candidate in connection with the Huntington's Program in 2020. As a result, the Company has a $10.0 million deferred revenue balance associated with the potential milestone payment. This deferral will be reversed upon payment of the milestone to Sanofi Genzyme. If the Company decides not to file an IND application for a product candidate in connection with the Huntington's Program, the Company will recognize that amount as revenue upon determining that the IND filing is no longer likely. The $20.0 million payable by the Company to Sanofi Genzyme in aggregate has been treated as consideration payable to a customer and therefore accounted for as a reduction of the transaction price.

During the three and six months ended June 30, 2019 the Company recognized $30.2 million and $31.6 million of revenue, respectively, associated with its collaboration with Sanofi Genzyme related to research and development services and committee obligations performed during the period. No amounts were recorded as revenue under the Sanofi Genzyme Collaboration Agreement in the three and six months ended June 30, 2020. As of June 30, 2020, there was $10.0 million of deferred revenue related to the Sanofi Genzyme Collaboration Agreement, which is classified as current in the accompanying balance sheet based on the period the services are expected to be delivered.

Costs incurred relating to the programs that Sanofi Genzyme had the option to license under the Sanofi Genzyme Collaboration Agreement consisted of internal and external research and development costs, which primarily included: salaries and benefits, lab supplies and preclinical research studies. These costs were included in research and development expenses in the Company's condensed consolidated statement of operations during the three and six months ended June 30, 2019.

AbbVie Tau Collaboration Agreement

Summary of Agreement

In February 2018, the Company entered into an exclusive collaboration and option agreement (the "AbbVie Tau Collaboration Agreement") with 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 Tau Collaboration Agreement, the Company and AbbVie 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 was comprised of a research period (the "Research Period"), a development period (the "Development Period"), and an exclusive license option (the "License Option"). The AbbVie Tau Collaboration Agreement included a non-refundable upfront payment to the Company of $69.0 million for services during the Research Period.

During the Research Period, each party agreed to identify up to five antibodies for inclusion in the collaboration. Subject to certain conditions and exceptions, the parties agreed to 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 was 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 was solely responsible for its costs and expenses during the Research Period. During a specified portion of the Research Period, AbbVie had the right to 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 agreed to 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 was obligated to use diligent efforts to conduct development activities, including IND application-enabling and Phase 1 clinical trial activities, for the Selected Research Compounds and corresponding Selected Product Candidates. The Company was solely responsible for the costs and expenses during the Development Period. During a specified portion of the Development Period (the "License Option Period"), AbbVie had the right to 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 agreed to provide a one-time payment of $75.0 million to the Company, and the Company agreed to 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 had certain obligations to complete any remaining research and development activities that had not been completed for any Research Compounds and Product Candidates.

The Company's research and development activities were to be conducted pursuant to the plans agreed to by the parties and overseen by a joint governance committee ("JGC") as detailed in the AbbVie Tau Collaboration Agreement. Any material amendment to the research or development plans were required to be mutually agreed to by the Company and AbbVie, which could be through the JGC.

Under the AbbVie Tau Collaboration Agreement, AbbVie agreed 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 was to be 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 had the option to 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 exercised a Cost-Sharing Option, the Company would either reimburse AbbVie for AbbVie's applicable development costs or, in the case of certain budget overruns,

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

Under the AbbVie Tau Collaboration Agreement, the Company was 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 was eligible to receive tiered, escalating royalties, in a range from a high-single digit to a mid-to-high teen (or, if the Company had 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 had 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 Tau Collaboration Agreement.

On July 28, 2020, the Company received notice from AbbVie Biotechnology Ltd ("AbbVie Biotechnology") of AbbVie Biotechnology's termination of the AbbVie Tau Collaboration Agreement. Subsequently, the parties mutually agreed that such termination would become effective as of August 3, 2020 (the "AbbVie Collaboration Termination Date"). Effective as of the AbbVie Collaboration Termination Date, the AbbVie Tau Collaboration Agreement has been terminated in its entirety, in accordance with its terms and conditions, subject to surviving rights and obligations thereunder. In connection with such termination, the Company is obligated to undertake certain transition activities, including transferring to AbbVie data and reports generated under the collaboration as well as any regulatory filings relating to certain compounds and product candidates investigated in the collaboration. As a result of the termination, the Company has been relieved of future research and development obligations under the collaboration. Exclusivity provisions restricting either party or any of its respective affiliates from directly or indirectly exploiting any vectorized antibody compound targeting a tau protein and restricting the Company, alone or jointly with any third party, from directly or indirectly exploiting specified antibodies targeting a tau protein have also terminated. Each party retains a royalty-free, exclusive license to the other's interest in certain intellectual property rights developed by or on behalf of either party under the collaboration (the "Joint IP") to exploit antibodies it contributed to the collaboration as well as a royalty-free, non-exclusive license to the Joint IP for any other purpose. Further, AbbVie has granted the Company, effective as of the AbbVie Collaboration Termination Date, a worldwide, royalty-free, transferable, sublicensable (though multiple tiers), exclusive license to AbbVie's interest in Joint IP to exploit research compounds or product candidates that were investigated under the collaboration and do not encode antibodies contributed by AbbVie or include active pharmaceutical ingredients owned by AbbVie or its affiliates, for all human diagnostic, prophylactic and therapeutic uses. The Company is not obligated to repay the upfront payment it received from AbbVie in connection with entering into the AbbVie Tau Collaboration Agreement but is no longer eligible to receive option payments, milestone payments or royalties thereunder.

Accounting Analysis

The Company assessed the promised goods and services under the AbbVie Tau Collaboration Agreement, in accordance with ASC 606, *Revenue from Contracts with Customers ("ASC 606")* and determined that the AbbVie Tau 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 Tau 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 estimated standalone selling price ("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, 2020, the Company recognized $1.1 million and $3.5 million, respectively, of revenue associated with the AbbVie Tau Collaboration related to the Research Services performed during the applicable period. During the three and six months ended June 30, 2019 the Company recognized $3.2 million and $4.9 million, respectively, of revenue associated with the AbbVie Tau Collaboration related to the Research Services performed during the applicable period. As of June 30, 2020, there was $47.2 million of deferred revenue related to the AbbVie Tau Collaboration Agreement, which is classified as either current or non-current in the accompanying condensed consolidated balance sheet based on the period the goods or services are expected to be delivered.

Costs incurred relating to the AbbVie Tau 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 condensed consolidated statement of operations during the three and six months ended June 30, 2020.

AbbVie Alpha Synuclein Collaboration Agreement

Summary of Agreement

In February 2019, the Company entered into an exclusive collaboration and option agreement ("the AbbVie Alpha-Synuclein Collaboration Agreement") with AbbVie, for the research, development and commercialization of AAV and other virus-based gene therapy products directed against pathological species of alpha-synuclein for the potential treatment of Parkinson's disease and other diseases characterized by the abnormal accumulation of misfolded alpha-synuclein protein ("synucleinopathies"). Under the AbbVie Alpha-Synuclein Collaboration Agreement, the Company and AbbVie 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 the alpha-synuclein protein. The collaboration was comprised of a research period (the "ASN Research Period"), an optional development period (the "ASN Development Period"), and an exclusive license option (the "ASN License Option"). The AbbVie Alpha-Synuclein Collaboration Agreement included a non-refundable upfront payment to the Company of $65.0 million for services during the ASN Research Period.

During the ASN Research Period, the Company was obligated to conduct research activities directed to constructing one or more virus vectors that encode antibodies designated by AbbVie (the "AbbVie Designated Antibodies") which initially are to be antibodies provided by AbbVie. The Company was obligated to use diligent efforts to conduct research activities to create research compounds ("ASN Research Compounds") and to develop product candidates containing or comprised of the ASN Research Compounds ("ASN Product Candidates"). The Company was solely responsible for the costs and expenses during the ASN Research Period. During a specified portion of the ASN Research Period, AbbVie had the right to exercise one or more of its exclusive development options to select up to a total of four ASN Research Compounds and their corresponding ASN Product Candidates to proceed to the ASN Development Period.

Upon AbbVie's exercise of an option to proceed to the ASN Development Period (an "ASN Development Option"), AbbVie agreed to pay the Company $80.0 million for the first ASN Research Compound and $30.0 million each for up to three additional ASN Research Compounds. During the ASN Development Period, the Company was obligated to use diligent efforts to conduct development activities, including IND application-enabling and Phase 1 clinical trial activities, for each selected ASN Research Compound and corresponding selected ASN Product Candidates. The Company was solely responsible for the costs and expenses during the ASN Development Period. During a specified portion of the ASN Development Period, AbbVie had the right to exercise its ASN License Option to further develop and commercialize all of the ASN Research Compounds and corresponding ASN Product Candidates. Upon AbbVie's exercise of its ASN License Option, the Company agreed to 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 ASN License Option, the Company had certain obligations to complete any remaining research and development activities that were not completed for any ASN Research Compounds and ASN Product Candidates.

The Company's research and development activities were to be conducted pursuant to the plans agreed to by the parties and overseen by a joint governance committee (or "ASN JGC") as detailed in the AbbVie Alpha-Synuclein Collaboration Agreement. Any material amendment to the research or development plans, however, were required to be mutually agreed to by the parties, which could be through the ASN JGC.

Under the AbbVie Alpha-Synuclein Collaboration Agreement, AbbVie agreed 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 ASN License Option, AbbVie was solely responsible for all development and commercialization activities relating to licensed compounds and licensed products at its sole cost and expense, subject to the Company's obligation to complete any remaining research and development activities set forth in the agreed-upon research and development plans.

Under the terms of the AbbVie Alpha-Synuclein Collaboration Agreement, the Company was eligible to receive (i) specified development and first-sale milestone payments for each licensed compound of up to an aggregate of $450.0 million in the case of a Parkinson's disease indication and up to $185.0 million in the case of the first indication other than Parkinson's disease and $92.5 million for a subsequent non-Parkinson's disease indication; (ii) specified commercial milestone payments based on net sales for all licensed products and all indications up to an aggregate of $500.0 million; and (iii) tiered, escalating royalties, in the mid-single digit percentage range for aggregate net sales of licensed products on a licensed compound by licensed compound basis, subject to potential reductions in certain circumstances.

On July 28, 2020, the Company received notice of the intent of AbbVie Inc., the parent company of AbbVie Ireland Unlimited Company ("AbbVie Ireland") to terminate the AbbVie Alpha-Synuclein Collaboration Agreement. On the AbbVie Collaboration Termination Date, Voyager received formal notice from AbbVie Ireland of its termination of the AbbVie Alpha-Synuclein Collaboration Agreement, and the parties mutually agreed that such termination would become effective as of the AbbVie Collaboration Termination Date. Effective as of the AbbVie Collaboration Termination Date, the AbbVie Alpha-Synuclein Collaboration Agreement has been terminated in its entirety, in accordance with its terms and conditions, subject to surviving rights and obligations thereunder. In connection with such termination, the Company is obligated to undertake certain transition activities including transferring to AbbVie data and reports generated under the collaboration as well as any regulatory filings relating to compounds and product candidates investigated in the collaboration. As a result of the termination, the Company has been relieved of future research and development obligations under the collaboration. Exclusivity provisions restricting either party or any of its respective affiliates from directly or indirectly exploiting any vectorized antibody compound targeting an alpha-synuclein protein and restricting the Company, alone or jointly with any third party, from directly or indirectly exploiting specified antibodies have also terminated. AbbVie retains a royalty-free, exclusive license to the Company's interest in the Joint IP to exploit antibodies AbbVie contributed to the collaboration. The Company otherwise retains a royalty-free, non-exclusive license to AbbVie's interest in the Joint IP. The Company is not obligated to repay the upfront payment it received from AbbVie in connection with entering into the AbbVie Alpha-Synuclein Collaboration Agreement but is no longer eligible to receive option payments, milestone payments, or royalties thereunder.

Accounting Analysis

The Company assessed the promised goods and services under the AbbVie Alpha-Synuclein Collaboration Agreement, in accordance with ASC 606, and determined that the AbbVie Alpha-Synuclein Collaboration Agreement includes the following performance obligations: (i) research services during the ASN Research Period (through the delivery of the final research report) including the conduct of research activities and provision of information to AbbVie to allow AbbVie to determine whether to exercise up to four ASN Development Options (collectively, the "ASN Research Services"), and (ii) a material right associated with the first ASN Development Option on the first ASN Research Compound and associated ASN Product Candidates ("ASN First Development Option Material Right"). The exercise of the first ASN Development Option provides AbbVie with (i) additional development services on a selected ASN Research Compound and (ii) the ability to exercise the ASN License Option. The Company has concluded the option provides a material right as the consideration paid by AbbVie upon exercise of the first ASN 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 ASN First Development Option Material Right is a separate performance obligation under ASC 606 as AbbVie is provided additional services and an ASN License Option for additional consideration that represents a significant discount from amounts that would otherwise be offered outside the context of the contract. The ASN 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 ASN 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 ASN License Option at an advantageous price.

The Company received a nonrefundable, upfront payment of $65.0 million as consideration under the AbbVie Alpha-Synuclein Collaboration Agreement, which represents the transaction price at inception. Additional consideration to be paid to the Company upon the exercise of the ASN Development and ASN 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 agreed upon ASN research plan. The ESP for the ASN First Development Option Material Right was determined based on the fees AbbVie would pay to exercise the ASN Development and ASN License Options, the estimated costs to perform the development services, inclusive of a reasonable profit margin, the estimated value of the ASN License Option using comparable transactions, and the probability that the ASN 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)
ASN Research Services	$ 23,768
ASN First Development Option Material Right	41,232
Total	$ 65,000

The Company recognizes the amounts associated with the ASN 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 ASN 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, 2020, the Company recognized $3.1 million and $4.3 million of revenue, respectively, associated with the AbbVie Alpha-Synuclein Collaboration related to the ASN Research Services performed during the period then ended. During the three and six months ended June 30, 2019, the Company recognized $0.2 million and $0.4 million of revenue, respectively, associated with the AbbVie Alpha-Synuclein Collaboration related to the ASN Research Services performed during the period then ended. As of June 30, 2020, there was $59.4 million of deferred revenue related to the AbbVie Alpha-Synuclein Collaboration Agreement, which is classified as either current or non-current in the accompanying condensed consolidated balance sheet based on the period the goods or services are expected to be delivered.

Costs incurred relating to the AbbVie Alpha-Synuclein 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 condensed consolidated statement of operations during the three and six months ended June 30, 2020.

Neurocrine Collaboration Agreement

Summary of Agreement

In March 2019, the Company entered into the Neurocrine Collaboration Agreement for the research, development and commercialization of certain of its AAV gene therapy products. Under the Neurocrine Collaboration

Agreement, the Company has agreed to collaborate on the conduct of four collaboration programs (the "Neurocrine Programs") which include: (i) the VY-AADC Program, (ii) the FA Program (collectively, the "Existing Programs"); and (iii) two programs to be determined by the Company and Neurocrine at a later date (the "Discovery Programs").

In June 2019, in conjunction with the termination of the Sanofi Genzyme Collaboration Agreement, the Company gained ex-U.S. rights to the FA Program. The Company's ex-U.S. rights to the FA Program were subsequently transferred to Neurocrine under the terms of the Neurocrine Collaboration Agreement. To facilitate the transfer of the ex-U.S. rights to the FA Program to Neurocrine, the Company and Neurocrine executed an amendment to the Neurocrine Collaboration Agreement (the "June 2019 Modification"), and Neurocrine paid $5.0 million to the Company. There were no other changes in pricing or scope of the obligations required to be performed under the Neurocrine Collaboration Agreement.

Under the terms of the Neurocrine Collaboration Agreement, the Company has agreed to collaborate with Neurocrine on, and to grant, exclusive, royalty-bearing, non-transferable, sublicensable licenses to certain of its intellectual property rights, for all human and veterinary diagnostic, prophylactic, and therapeutic uses, for the research, development, and commercialization of gene therapy products (the "Collaboration Products") on a worldwide basis under (i) the VY-AADC Program; (ii) the FA Program; and (iii) each Discovery Program.

Pursuant to development plans to be agreed by the parties, which will be overseen by a joint steering committee ("JSC"), the Company has operational responsibility, subject to certain exceptions, for the conduct of each Neurocrine Program prior to the occurrence of a specified event for such Neurocrine Program (a "Transition Event"), as described below, and is required to use commercially reasonable efforts to develop the corresponding Collaboration Products. Neurocrine has agreed to be responsible for all costs incurred by the Company in conducting these activities for each Neurocrine Program, in accordance with an agreed budget for each Neurocrine Program. If the Company breaches its development responsibilities or in certain circumstances upon a change in control, Neurocrine has the right but not the obligation to assume the activities under such Neurocrine Program.

Upon the occurrence of a Transition Event, Neurocrine has agreed to assume responsibility for development, manufacturing and commercialization activities for such Neurocrine Program from the Company and to pay milestones and royalties on future net sales as described further below. The Transition Events are (i) with respect to the VY-AADC Program, the Company's receipt of topline data for the RESTORE-1 Phase 2 clinical trial for VY-AADC (NBIb-1817); (ii) with respect to the FA Program, the Company's receipt of topline data for the initial Phase 1 clinical trial for a FA Program product candidate; and (iii) with respect to each Discovery Program, the preparation by the Company and the approval by Neurocrine of an IND application to be filed with the Food and Drug Administration (the "FDA") by Neurocrine for the first development candidate in such Discovery Program. For each Existing Program, the Company has the option (the "Co-Co Option") to co-develop and co-commercialize such Neurocrine Program upon the occurrence of a specified event (a "Co-Co Trigger Event"). Should the Company elect to exercise its Co-Co Option, the Company has agreed to enter into a cost- and profit-sharing arrangement with Neurocrine (a "Co-Co Agreement"), whereby it has agreed to jointly develop and commercialize Collaboration Products for such Neurocrine Existing Program ("Co-Co Products") and share in its costs, profits and losses, and the Company agrees to forfeit certain milestones and royalties on net sales in the United States during the effective period of the applicable Co-Co Agreement. The Co-Co Trigger Events are (i) with respect to the VY-AADC Program, the Company's receipt of topline data for the ongoing RESTORE-1 Phase 2 clinical trial for VY-AADC (NBIb-1817) and (ii) with respect to the FA Program, the receipt of topline data for the initial Phase 1 clinical trial for a FA Program product candidate.

Subject to exceptions specified in the Neurocrine Collaboration Agreement, profits and losses under the Company's Co-Co Option are agreed to be allocated (i) 50% to Neurocrine and 50% to the Company for a Collaboration Product from the VY-AADC Program and (ii) 60% to Neurocrine and 40% to the Company for a Collaboration Product from the FA Program; provided, however, that Neurocrine may elect, within a specified period following the acceptance for filing of a biologics license application from the FDA, to pay a $35.0 million rate-shifting fee to the Company to change the allocation for the VY-AADC Program to 55% to Neurocrine and 45% to the Company. The parties have agreed that each Co-Co Agreement will provide the Company the right to terminate for any reason upon prior written notice to Neurocrine and Neurocrine the right to terminate in certain circumstances upon change of control.

The Company's research and development activities under the Neurocrine Collaboration Agreement are to be conducted pursuant to plans agreed to by the parties, on a program-by-program basis, and overseen by the JSC, as detailed in the Neurocrine Collaboration Agreement.

The parties have committed to agree on a list of up to eight target genes (the "Targets") from which Neurocrine has the right to nominate Targets for the two Discovery Programs. The Targets nominated for the Discovery Programs must be approved by a consensus of the JSC or the executive officers.

The Neurocrine Collaboration Agreement provides for an upfront non-refundable payment of $115.0 million, as well as for aggregate development and regulatory milestone payments from Neurocrine to the Company for Collaboration Products under (i) the VY-AADC Program of up to $170.0 million; (ii) the FA Program of up to $195.0 million, and (iii) each of the two Discovery Programs of up to $130.0 million per Discovery Program. The Company may be entitled to receive aggregate commercial milestone payments for each Collaboration Product of up to $275.0 million, subject to an aggregate cap on commercial milestone payments across all Neurocrine Programs of $1.1 billion. Furthermore, in connection with the Neurocrine Collaboration Agreement, Neurocrine has purchased 4,179,728 shares of the Company's common stock at a price of $11.9625 per share, for an aggregate purchase price of $50.0 million.

Neurocrine has also agreed to pay the Company royalties, based on future net sales of the Collaboration Products. Such royalty percentages, for net sales in and outside the United States, as applicable, range (i) for the VY-AADC Program, from the mid-teens to low thirties and the low-teens to low twenties, respectively; (ii) for the FA Program, from the low-teens to high-teens and high-single digits to mid-teens, respectively; and (iii) for each Discovery Program, from the high-single digits to mid-teens and mid-single digits to low-teens, respectively. On a country-by-country and program-by-program basis, royalty payments would commence on the first commercial sale of a Collaboration Product and terminate on the later of (a) the expiration of the last patent covering the Collaboration Product or its method of use in such country, (b) ten years from the first commercial sale of the Collaboration Product in such country and (c) the expiration of regulatory exclusivity in such country, or the Royalty Term. Royalty payments may be reduced by up to 50% in specified circumstances, including expiration of patents rights related to a Collaboration Product, approval of biosimilar products in a given country or required payment of licensing fees to third parties related to the development and commercialization of any Collaboration Product. Additionally, the licenses granted to Neurocrine shall automatically convert to fully paid-up, non-royalty bearing, perpetual, irrevocable, exclusive licenses on a country-by-country and product-by-product basis upon the expiration of the Royalty Term applicable to such Collaboration Product in such country.

Under the terms of the Neurocrine Collaboration Agreement and subject to specified exceptions therein, each party owns the entire right, title and interest in and to all intellectual property rights made solely by its employees or agents in the course of the collaboration. The parties jointly own all rights, title and interest in and to all intellectual property rights made or invented jointly by employees or agents of both parties.

During the term of the Neurocrine Collaboration Agreement, neither party nor any of its respective affiliates is permitted to directly or indirectly exploit any AAV-based gene therapy products directed to a Target to which a Collaboration Product is directed, subject to specified exceptions including the parties' conduct of basic research activities.

Unless earlier terminated, the Neurocrine Collaboration Agreement expires on the later of (i) the expiration of the last to expire royalty term with respect to a Collaboration Product in all countries in the relevant territory or (ii) the expiration or termination of all Co-Co Agreements. Neurocrine may terminate the Neurocrine Collaboration Agreement in its entirety or on a program-by-program or country-by-country basis by providing at least (x) 180-day advance notice if such notice is provided prior to the first commercial sale of the Collaboration Product to which the termination applies or (y) one-year advance notice if such notice is provided after the first commercial sale of the Collaboration Product to which the termination applies. The Company may terminate the Neurocrine Collaboration Agreement, subject to specified conditions, if Neurocrine challenges the validity or enforceability of certain of the Company's intellectual property rights. Subject to a cure period, either party may terminate the Neurocrine Collaboration Agreement in the event of a material breach by the other party in whole or in part, subject to specified conditions.

Upon termination in certain cases, Neurocrine has agreed to grant to the Company licenses to certain Neurocrine intellectual property, subject to a negotiation between the parties to establish royalty rates for use of such

intellectual property. In the event of a breach by the Company with respect to a Neurocrine Program, if such termination were to occur after a Transition Event, then (i) if a Co-Co Agreement is in effect with respect to such program, Neurocrine can terminate the Co-Co Agreement for such program and the Company would no longer have co-development and co-commercialization rights with respect to the Collaboration Product and (ii) subject to any license agreements, Neurocrine would no longer have any obligations with respect to any Collaboration Products resulting from such program.

Accounting Analysis

At inception, the Neurocrine Collaboration Agreement included the following performance obligations: (i) research and development services for each Existing Program combined with a development and commercialization license for each such program and (ii) research and development services for each Discovery Program combined with a development and commercialization license for each program. The research services and license on a program by program basis are not distinct as Neurocrine cannot benefit from such license on its own or from other resources commonly available in the industry, without the corresponding research services due to the unique and specialized expertise of the Company that is not readily available in the marketplace.

The Company has identified $92.4 million of fixed transaction price consisting of the $115.0 million upfront fee and $5.0 million payment from the June 2019 Modification, offset by a discount of $27.6 million related to the $50.0 million equity investment of 4,179,728 shares when measured at fair value on the date of issuance. The Company is also entitled to reimbursement of costs incurred by the Company prior to the Transition Events associated with each Neurocrine Program. These amounts are determinable based on program plans and budgets, and the Company has a contractual right to the payment of costs incurred under the agreed upon program plans. The Company has utilized the most likely amount approach and estimated the expected cost reimbursement to be $431.1 million at inception. The Company has concluded that these amounts do not require a constraint and are included in the transaction price at inception. The Company considers this estimate at each reporting date and updates the estimate based on information available. During the second quarter of 2020, the Company has further revised the estimate of the expected reimbursement to $340.4 million during the second quarter of 2020 based on current expectations. Additional consideration to be paid to the Company upon reaching certain milestones are excluded from the transaction price at inception due to the uncertainty of achieving the development and regulatory milestones.

The Company has allocated the fixed transaction price to the separate performance obligations based on the relative standalone selling price of each performance obligation or in the case of certain variable consideration to one or more performance obligations. The estimated standalone selling prices for performance obligations, that include a license and research services, were developed using the estimated selling price of the license, using comparable and market data, and an estimate of the overall effort to perform the research services along with a reasonable profit for research services.

The Company has concluded that the variable consideration related to the cost reimbursement of each program will be allocated to each respective program as the cost reimbursement relates specifically to the respective program services being performed under the Neurocrine Collaboration. The reimbursement of research services is considered to be at a market rate and the allocation of the fixed consideration to all of the performance obligations depicts the estimated amounts in which it would expect to receive for these obligations, absent the variable consideration related to

the research reimbursement. The total variable consideration allocated to each program related to the expected cost reimbursement was as follows at June 30, 2020:

Performance Obligation	Amount
	(in thousands)
Variable Consideration	
VY-AADC Program	$ 83,983
FA Program	113,033
Discovery Program 1	72,164
Discovery Program 2	71,262
Total	$ 340,442

Based on the relative standalone selling price allocation, the allocation of the transaction price, exclusive of the variable consideration allocated to the individual performance obligations, to the separate performance obligations was as follows:

Performance Obligation	Amount
	(in thousands)
Fixed Consideration	
VY-AADC Program	$ 80,373
FA Program	6,005
Discovery Program 1	3,002
Discovery Program 2	3,002
Total	$ 92,382

The Company recognizes the transaction price associated with each performance obligation 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.

During the three and six months ended June 30, 2020, the Company recognized $24.5 million and $38.9 million of revenue, respectively, associated with its collaboration with Neurocrine related to research and development services performed during the period and the corresponding cost reimbursement receivable. During the three and six months ended June 30, 2019, the Company recognized $12.5 million and $14.4 million of revenue, respectively, associated with its collaboration with Neurocrine related to research and development services performed during the period and the corresponding cost reimbursement receivable. As of June 30, 2020, there was $50.1 million of deferred revenue related to the Neurocrine Collaboration Agreement, which is classified as either current or non-current in the accompanying condensed consolidated balance sheet based on the period the services are expected to be delivered. Additionally, as of June 30, 2020, there was $12.7 million of collaboration and unbilled receivables related to reimbursable costs expected to be received from Neurocrine for research and development services performed.

Costs incurred relating to the Collaboration Programs consist of internal and external research and development costs, which primarily include: salaries and benefits, lab supplies, preclinical research studies, clinical studies, consulting services, and commercial development. These costs are included in research and development expenses in the Company’s condensed consolidated statement of operations during the three and six months ended June 30, 2020.

The Company incurred approximately $0.8 million of costs to obtain the Neurocrine Collaboration Agreement which were payable only upon the close of the deal and therefore considered incremental costs of obtaining a contract with a customer and capitalized. The costs are recorded in prepaid expenses and other non-current assets and are being amortized over the period in which the research services will be provided.

Other Agreements

The Company has entered into various agreements with contract research organizations and institutions to license intellectual property. In consideration for the rights licensed under such agreements, the Company generally made upfront payments, which were recorded as research and development expense as the acquired technologies were considered in-process research and development. The license agreements obligate the Company to make additional payments that are contingent upon specific clinical trial and regulatory approval milestones being achieved as well as royalties on future product sales. The agreements to license intellectual property include potential milestone payments that are dependent upon the development of products licensed under the agreements and contingent upon the achievement of clinical trial or regulatory approval milestones. To date, the Company reached a milestone related to first patient dosing on the RESTORE-1 Phase 2 clinical trial which resulted in a $0.1 million milestone payment to one of its licensors. The Company can generally terminate the license agreements upon 30 to 90 days' prior written notice.

Additionally, certain license agreements require the Company to reimburse the licensor for certain past and ongoing patent related expenses.

During the year ended December 31, 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 to the Company 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 the year ended December 31, 2017, the Company earned a milestone payment of $1.0 million. 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 condensed consolidated balance sheet.

Litigation

The Company is not a party to any material legal matters or claims and did not have contingency reserves established for any litigation liabilities as of June 30, 2020 or December 31, 2019.

9. Stock-based compensation

Stock-Based Compensation Expense

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
	(in thousands)			
Research and development	$ 1,764	$ 3,256	$ 3,449	$ 4,671
General and administrative	2,095	1,998	4,451	4,100
Total stock-based compensation expense	$ 3,859	$ 5,254	$ 7,900	$ 8,771

Stock-based compensation expense by type of award included within the condensed consolidated statements of operations and comprehensive loss was as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
	(in thousands)			
Stock options	$ 2,930	$ 4,528	$ 6,138	$ 7,304
Restricted stock awards and units	864	668	1,605	1,351
Employee stock purchase plan awards	65	58	157	116
Total stock-based compensation expense	$ 3,859	$ 5,254	7,900	8,771

Restricted Stock Units

A summary of the status of and changes in unvested restricted stock unit activity under the Company's equity award plans for the six months ended June 30, 2020 was as follows:

	Units	Weighted Average Grant Date Fair Value Per Unit
Unvested restricted stock units as of December 31, 2019	455,404	12.16
Granted	448,929	$ 12.83
Vested	(130,003)	11.02
Forfeited	(64,600)	$ 10.66
Unvested restricted stock units as of June 30, 2020	709,730	$ 12.93

Stock-based compensation of restricted stock units is based on the fair value of the Company's common stock on the date of grant and is recognized over the vesting period. The weighted average fair value of restricted stock units granted to employees during the three and six months ended June 30, 2020 was $8.05 and $12.83 per share, respectively. The weighted average fair value of restricted stock units granted to employees during the three and six months ended June 30, 2019 was $20.74 and $10.91 per share, respectively. The restricted stock units granted in the three and six months ended June 30, 2020 vest in equal amounts, annually over three years. The expense related to restricted stock units granted to employees was $0.9 million and $1.6 million for the three and six months ended June 30, 2020, respectively. The expense related to restricted stock units granted to employees was $0.7 million and $1.4 million for the three and six months ended June 30, 2019, respectively.

As of June 30, 2020, the Company had unrecognized stock-based compensation expense related to its unvested restricted stock units of $7.7 million, which is expected to be recognized over the remaining average vesting period of 2.3 years.

Stock Options

The following is a summary of stock option activity for the six months ended June 30, 2020:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2019	5,317,326	$ 15.98		
Granted	1,147,215	$ 12.33		
Exercised	(163,513)	$ 10.31		
Cancelled or forfeited	(407,853)	$ 16.59		
Outstanding at June 30, 2020	5,893,175	$ 15.38	7.5	$ 5,378
Exercisable at June 30, 2020	2,988,988	$ 15.55	6.4	$ 3,334

As of June 30, 2020, the Company had unrecognized stock-based compensation expense related to its unvested stock options of $26.3 million which is expected to be recognized over the remaining weighted-average vesting period of 2.7 years.

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,	
	2020	2019
Unvested restricted common stock awards	176,471	235,294
Unvested restricted common stock units	709,730	402,782
Outstanding stock options	5,893,175	5,239,535
Total	6,779,376	5,877,611

Basic net loss per share for the six months ended June 30, 2020 and 2019, is the same as diluted net loss per share as shown on the Company's condensed consolidated statement of operations.

11. Related-party transactions

Historically, the Company has received consulting and management services from one of its investors. During the three and six months ended June 30, 2020, there were no consulting and management services provided by this investor. During the three and six months ended June 30, 2019 the total amount of services provided by this investor was de minimis. As of June 30, 2020, there were no amounts payable related to consulting and management service fees provided by this investor.

Additionally, during the three and six months ended June 30, 2020, the Company received board and scientific advisory services from two of its prior executives, Steven M. Paul, M.D., the Company's former President and Chief Executive Officer, and Dinah Sah, Ph.D., the Company's former Chief Scientific Officer. The total amount of fees paid to Dr. Paul for services provided during each of the three and six months ended June 30, 2020 and 2019 was $50 thousand and $0.1 million, respectively. The total amount of fees paid to Dr. Sah for services provided during the three and six months ended June 30, 2020 was $0.1 million and $0.2 million, respectively.

Under the collaboration agreement, the Company and Neurocrine have agreed to conduct research, development and commercialization of certain of the Company's AAV gene therapy products (Note 8). Amounts due from Neurocrine are reflected as related party collaboration receivables. As of June 30, 2020, the Company had approximately $12.7 million in related party collaboration receivable associated with Neurocrine.

12. Subsequent Events

On July 28, 2020, the Company received notice from AbbVie Biotechnology of (i) AbbVie Biotechnology's termination of the AbbVie Tau Collaboration Agreement and (ii) the intention of AbbVie Inc., the parent of AbbVie Ireland, to terminate the AbbVie Alpha-Synuclein Collaboration Agreement. On the AbbVie Collaboration Termination Date, the Company received formal notice from AbbVie Ireland of AbbVie Ireland's termination of the AbbVie Alpha-Synuclein Collaboration Agreement. In each case, AbbVie exercised its right to terminate for convenience in accordance with the terms and conditions of the applicable agreement, and the parties have mutually agreed that each termination became effective as of the AbbVie Collaboration Termination Date.

AbbVie Tau Collaboration Agreement

Effective as of the AbbVie Collaboration Termination Date, the AbbVie Tau Collaboration Agreement has been terminated in its entirety, in accordance with its terms and conditions, subject to surviving rights and obligations thereunder. In connection with such termination, the Company is obligated to undertake certain transition activities, including transferring to AbbVie data and reports generated under the collaboration as well as any regulatory filings relating to certain compounds and product candidates investigated in the collaboration. As a result of the termination, the Company has been relieved of future research and development obligations under the collaboration. Exclusivity provisions restricting either party or any of its respective affiliates from directly or indirectly exploiting any vectorized antibody compound targeting a tau protein and restricting the Company, alone or jointly with any third party, from directly or indirectly exploiting specified antibodies targeting a tau protein have also terminated. Each party retains a royalty-free, exclusive license to the other's interest in the Joint IP to exploit antibodies it contributed to the collaboration as well as a royalty-free, non-exclusive license to the Joint IP for any other purpose. Further, AbbVie has granted the Company, effective as of the AbbVie Collaboration Termination Date, a worldwide, royalty-free, transferable, sublicensable (though multiple tiers), exclusive license to AbbVie's interest in Joint IP to exploit research compounds or product candidates that were investigated under the collaboration and do not encode antibodies contributed by AbbVie or include active pharmaceutical ingredients owned by AbbVie or its affiliates, for all human diagnostic, prophylactic and therapeutic uses. The Company is not obligated to repay the upfront payment it received from AbbVie in connection with entering into the AbbVie Tau Collaboration Agreement but is no longer eligible to receive option payments, milestone payments or royalties thereunder.

AbbVie Alpha-Synuclein Collaboration Agreement

Effective as of the AbbVie Collaboration Termination Date, the AbbVie Alpha-Synuclein Collaboration Agreement has been terminated in its entirety, in accordance with its terms and conditions, subject to surviving rights and obligations thereunder. In connection with such termination, the Company is obligated to undertake certain transition activities including transferring to AbbVie data and reports generated under the collaboration as well as any regulatory filings relating to compounds and product candidates investigated in the collaboration. As a result of the termination, the Company has been relieved of future research and development obligations under the collaboration. Exclusivity provisions restricting either party or any of its respective affiliates from directly or indirectly exploiting any vectorized antibody compound targeting an alpha-synuclein protein and restricting the Company, alone or jointly with any third party, from directly or indirectly exploiting specified antibodies have also terminated. AbbVie retains a royalty-free, exclusive license to the Company's interest in the Joint IP to exploit antibodies AbbVie contributed to the collaboration. The Company otherwise retains a royalty-free, non-exclusive license to AbbVie's interest in the Joint IP. The Company is not obligated to repay the upfront payment it received from AbbVie in connection with entering into the AbbVie Alpha-Synuclein Collaboration Agreement but is no longer eligible to receive option payments, milestone payments, or royalties thereunder.

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, 2019, which was filed with the Securities and Exchange Commission, or the SEC, on March 3, 2020.

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, or the Exchange Act. 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

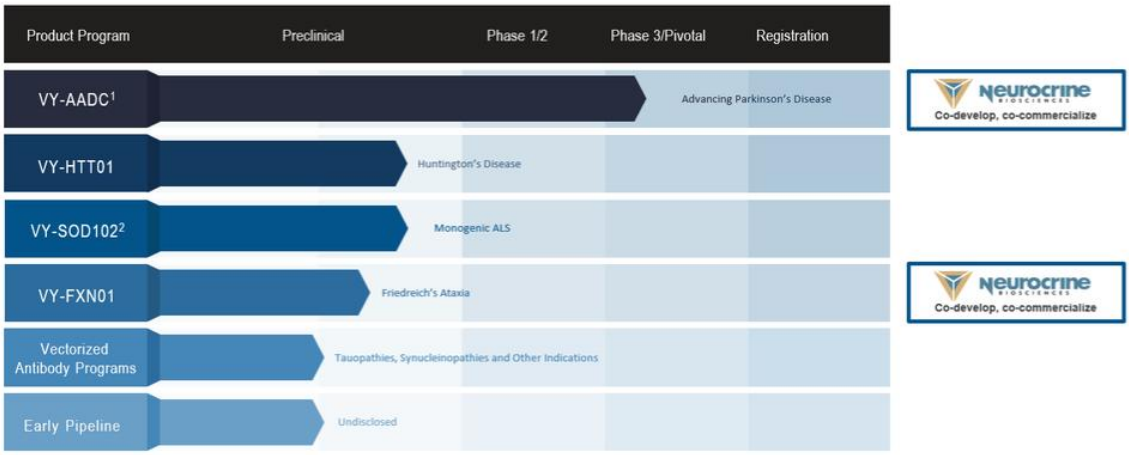
We are a clinical-stage gene therapy company focused on developing life-changing treatments for patients suffering from severe neurological diseases. We focus on neurological diseases where we believe an adeno-associated virus, or AAV, gene therapy approach that either increases or decreases the production 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. In addition to our capsid optimization efforts, we leverage novel delivery paradigms, established routes of administration, and advances in dosing techniques to optimize delivery of our AAV gene therapies to target tissues, regions and cell types that are critical to the disease of interest. We believe we can achieve this directly, with targeted infusions to discrete regions of the brain or spinal cord, or systemically, in conjunction with our novel capsids.

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 specific geographies

with collaborators, as we have demonstrated through our collaborations, including those with Sanofi Genzyme Corporation, which we refer to as Sanofi Genzyme, AbbVie Biotechnology Ltd. and AbbVie Ireland Unlimited Company, which we collectively refer to as AbbVie, and Neurocrine Biosciences, Inc., which we refer to as Neurocrine. 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 our strategic collaborations, including our collaboration with Sanofi Genzyme, or the Sanofi Genzyme Collaboration, which commenced in February 2015 and was terminated in June 2019, our collaboration with AbbVie focusing on tau-related diseases, or the AbbVie Tau Collaboration, which commenced in February 2018 and was terminated effective August 3, 2020 pursuant to notice we received from AbbVie on July 28, 2020, our collaboration with AbbVie focusing on pathological species of alpha-synuclein, or the AbbVie Alpha-Synuclein Collaboration, which commenced in February 2019 and was terminated effective August 3, 2020 , and our collaboration with Neurocrine, or the Neurocrine Collaboration, which commenced in March 2019.

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



(1) The RESTORE-1 Phase 2 clinical trial and RESTORE-2 Phase 3 clinical trial are expected to constitute pivotal trials for VY-AADC (NBIb-1817)
(2) Voyager intends to seek a partner to advance

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

We are evaluating our most advanced clinical candidate, VY-AADC (which Neurocrine refers to as NBIb-1817), or VY-AADC (NBIb-1817), for the treatment of Parkinson's disease, through the Neurocrine Collaboration in the RESTORE-1 Phase 2, randomized, double-blind, sham-surgery controlled trial evaluating the safety and efficacy of VY-AADC (NBIb-1817) for the treatment of moderate to advanced Parkinson's disease patients with motor fluctuations. In June 2018, the FDA granted RMAT designation for the VY-AADC Program gene therapy treatment, which provides for an enhanced level of interactions between the company sponsor and the FDA throughout the development program. The designation was based on our Phase 1b clinical data with VY-AADC (NBIb-1817). The FDA has also granted fast-track designation for VY-AADC (NBIb-1817).

VY-AADC (NBIb-1817) Phase 1 Clinical Development

We are evaluating the delivery of VY-AADC (NBIb-1817) in a transfrontal (i.e., top of the head) surgical delivery route in a Phase 1b clinical trial, which we refer to as PD-1101, and we are exploring the delivery of VY-AADC (NBIb-1817) using a posterior trajectory (i.e., back of the head) surgical delivery route in a Phase 1 clinical trial, which we refer to as PD-1102. PD-1101 is an open-label, dose-ranging, Phase 1b clinical trial for VY-AADC (NBIb-1817) to evaluate safety and efficacy. We enrolled 15 patients with advanced Parkinson's disease and assessed increased volume or concentration of VY-AADC (NBIb-1817) in three separate cohorts consisting of five patients in each cohort. PD-1102 is a separate, open-label Phase 1 clinical trial for VY-AADC (NBIb-1817) that enrolled eight patients with advanced Parkinson's disease. We have completed enrollment in both PD-1101 and PD-1102 and continue to follow patients in these trials. Preliminary data from both trials demonstrate that VY-AADC (NBIb-1817) has been well-tolerated, and that administration with VY-AADC (NBIb-1817) improved patients' motor function and quality of life as measured by standard scores and measures used in Parkinson's disease trials.

Results from PD-1101 have been reported beginning in late 2016 and most recently in November 2018. In May 2019, we provided 12-month results from PD-1102. We and Neurocrine plan to present the final three-year data on all three cohorts of the PD-1101 Phase 1b trial, as well as two-year data from the PD-1102 Phase 1 trial, at the Movement Disorder Society (MDS) Virtual Congress 2020 being held September 12-16, 2020.

VY-AADC (NBIb-1817) RESTORE-1 and RESTORE-2 Program

In December 2018, we announced randomization of the first patient in the RESTORE-1 Phase 2, randomized, double-blind, sham-surgery controlled trial evaluating the safety and efficacy of VY-AADC (NBIb-1817) for the treatment of moderate to advanced Parkinson's disease in patients with motor fluctuations. We received written feedback from the FDA, including FDA guidance received during the Type B meeting, that in a disease such as Parkinson's, two adequate and well-controlled clinical trials are suggested. Based upon feedback received from the FDA, we and Neurocrine have amended the RESTORE-1 clinical trial protocol to support a future registration filing, if successful, for VY-AADC (NBIb-1817) for the treatment of Parkinson's disease in the United States. The protocol amendments include increasing the planned enrollment to approximately 85 patients from the previously planned 42 patients, and adjusting future enrollment in the trial to randomize patients 2:1 to VY-AADC (NBIb-1817) or sham surgery, respectively, as compared to the previous 1:1 randomization. The eligibility criteria remain substantially the same: the trial is potentially available to patients who have been diagnosed with Parkinson's disease for at least four years, are not responding adequately to oral medications, and have at least three or more hours of OFF time during the day as measured by a validated self-reported patient diary. The protocol amendments are anticipated to facilitate enrollment and patient convenience, but implementation of the protocol amendments will lengthen the trial enrollment period. As previously announced, trial sites had temporarily suspended patient screening and enrollment activity in response to the COVID-19 pandemic and the implementation of these previously disclosed protocol amendments. We and Neurocrine expect patient screening to resume during the second half of 2020 at certain clinical sites in the RESTORE-1 trial.

For the RESTORE-1 Phase 2 clinical trial, we have selected a dose of up to 2.5×10^{12} vector genomes, or vg, 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 PD-1101 when considering the higher volume administered with the posterior trajectory and vector produced using the baculovirus system.

The primary efficacy endpoint of the RESTORE-1 Phase 2 trial is the mean improvement from baseline to 12 months in good ON time as measured by a validated self-reported patient diary at 12 months compared to sham surgery. Secondary endpoints include mean improvement in diary OFF time, other motor function and quality of life measures from the Unified Parkinson's Disease Rating Scales (UPDRS-II and -III scores), assessments from the Parkinson's Disease Questionnaire (PDQ-39), and patient's global function as measured by the proportion of participants with improvement on the Clinical Global Impression (CGI) score. The trial will also measure non-motor symptoms from the Non-Motor Symptom Scale (NMSS), as well as safety.

Changes in patients' daily doses of oral levodopa and related medications will also be recorded. Biomarker data collected during the RESTORE-1 Phase 2 trial will include measurements of the coverage of the putamen, the specific

region of the brain targeted with VY-AADC (NBIb-1817), and measurements of AADC enzyme expression and activity in the putamen measured by positron emission tomography using 18-F fluorodopa.

We and Neurocrine currently expect to initiate the RESTORE-2 Phase 3 clinical trial in the first half of 2021. We anticipate that, if positive, results from the RESTORE-1 Phase 2 clinical trial and the planned RESTORE-2 Phase 3 clinical trial could potentially form the basis for submission of a biologics license application, or BLA, to the FDA for VY-AADC (NBIb-1817) for the treatment of Parkinson's disease.

As part of the IND for VY-AADC (NBIb-1817), the chemistry, manufacturing, and controls section included data demonstrating comparability between VY-AADC (NBIb-1817) using our baculovirus/Sf9 manufacturing process and VY-AADC (NBIb-1817) produced using a mammalian cell system consisting of triple-transfection of HEK293 cells, which was used in our two Phase 1 clinical trials. Both were produced under cGMP. Our baculovirus/Sf9 manufacturing process is designed for production of AAV vectors at clinical and commercial scale, with the potential for increased yields and efficient scalability compared with mammalian-based systems. We have demonstrated that this production platform change resulted in comparable vector quality and activity. We are using VY-AADC (NBIb-1817) manufactured in our baculovirus/Sf9 system in the RESTORE-1 Phase 2 clinical trial and the planned RESTORE-2 Phase 3 clinical trial.

Preclinical Pipeline Programs

We are pursuing additional product candidates in the preclinical stages of development, including treatment programs for Huntington's disease, ALS, Friedreich's ataxia, tau-related neurodegenerative diseases, and diseases characterized by the abnormal accumulation of misfolded alpha-synuclein protein, or synucleinopathies.

In June 2019, we and Sanofi Genzyme executed a termination agreement, or the Sanofi Genzyme Termination Agreement, to terminate our collaboration agreement with Sanofi Genzyme, or the Sanofi Genzyme Collaboration Agreement. Under the terms of the Sanofi Genzyme Termination Agreement, Sanofi Genzyme relinquished its rights to the exclusive license options to VY-HTT01 for Huntington's disease, or the Huntington's Program, VY-FXN01 for Friedreich's ataxia, or the FA Program, and a future program to be designated by Sanofi Genzyme, or the Future Program. We have been relieved of our obligations to perform the research and development services under those programs through completion of the respective proof of principle human clinical studies, or POP Studies. As a result, we gained worldwide rights to the Huntington's Program, and ex-U.S. rights to the FA Program. In accordance with our Collaboration and License Agreement with Neurocrine, or the Neurocrine Collaboration Agreement, the ex-U.S. rights to the FA Program then passed to Neurocrine. Additionally, we and Sanofi Genzyme entered into the Amended and Restated Option and License Agreement related to certain AAV capsids, or the Amended Capsid Agreement. Under the Amended Capsid Agreement, Sanofi Genzyme obtains exclusive option rights to select up to two novel AAV capsids owned or controlled by us for exclusive use for up to an aggregate of two non-central nervous system, or non-CNS indications.

Under the Sanofi Genzyme Termination Agreement, we made a $10.0 million upfront payment to Sanofi Genzyme and have agreed to pay a $10.0 million milestone payment to Sanofi Genzyme within fifteen days of the filing of an IND application for a product candidate incorporating certain intellectual property rights developed under or substantially related to, the Huntington's Program, which we refer to as a Post-Termination HD Product. We have agreed to pay Sanofi Genzyme (i) 50% of any income received from sublicensing arrangements related to Post-Termination HD Products in excess of specified thresholds and entered into prior to (a) the filing of an IND application for a Post-Termination HD Product or (b) the dosing of the first patient in a clinical trial for a Post-Termination HD Product in the United States or certain European countries, respectively and (ii) a low-double digit percentage of any income received from sublicensing arrangements outside the United States related to products incorporating intellectual property rights developed under, or substantially related to, the FA Program, which we refer to as Post-Termination FA Products, that are in excess of a specified threshold and entered into prior to the dosing of the first patient in a clinical trial for a Post-Termination FA Product in the United States or certain European countries, in each case, subject to certain limitations. We have also agreed to pay low-single-digit royalties on net sales of Post-Termination HD Products. Under the Sanofi Genzyme Collaboration Agreement, we had rights to certain in-kind services. As of the effective date of the Sanofi

Genzyme Termination Agreement, we waived our right to approximately $0.4 million in unused in-kind services, we have relinquished our rights to the spinal muscular atrophy program, and we no longer have the right to receive any option payments, regulatory or commercial milestone payments or royalties from Sanofi Genzyme under the Sanofi Genzyme Collaboration Agreement.

VY-HTT01 is our clinical gene therapy candidate for the treatment of Huntington's disease. VY-HTT01 is composed of an AAV capsid (AAV1) and a proprietary transgene that harnesses the RNA interference pathway to selectively knock down, or reduce, levels of HTT mRNA. We recently completed IND-enabling preclinical studies and are in the process of finalizing an IND application for VY-HTT01 for the treatment of Huntington's disease which we expect to file with the FDA during the second half of 2020.

In non-human primate studies, one-time administration of VY-HTT01 resulted in robust and durable reduction of HTT mRNA and protein with knock-down stabilization between 6- and 12-months, and widespread distribution of VY-HTT01 vector genome across the striatum and cortex. VY-HTT01 treatment demonstrated robust reduction of HTT mRNA and protein in the YAC128 and BACHD transgenic mouse models of Huntington's disease, with significant improvements in motor function. We plan to present preclinical data from the IND-enabling studies at a future scientific congress in the first half of 2021.

Following clearance of the IND by the FDA, we expect to begin the first-in-human clinical trial of VY-HTT01 in Huntington's disease patients.

As part of the Neurocrine Collaboration, we are also developing VY-FXN01 for the treatment of Friedreich's ataxia, a debilitating neurodegenerative disease resulting in poor coordination of legs and arms, progressive loss of the ability to walk, generalized weakness, loss of sensation, scoliosis, diabetes and cardiomyopathy as well as impaired vision, hearing and speech. VY-FXN01 is currently in preclinical development. We and Neurocrine are in the process of identifying a lead candidate which will comprise an optimal capsid, promoter, and FXN transgene. We are completing several AAV capsid screening experiments to identify capsids that effectively distribute to disease target tissues in a desired manner following intravenous injection. Criteria for evaluating these capsids include safety, overall level of transgene expression achieved, distribution of transgene expression and the specific cell types transduced. In addition, we are optimizing the promoter for VY-FXN01. To evaluate the therapeutic potential of our vectors, we have conducted testing in a new genetic mouse model of Friedreich's ataxia. In this preclinical model of Friedreich's ataxia, our gene therapy candidates durably improved sensory function, and rescued the Friedreich's ataxia phenotype based on multiple functional tests. In physiological and behavioral assays, our gene therapy candidates demonstrated dose-dependent and durable responses for more than 10 months after a single administration, preventing central and peripheral disease progression. We also have a significant effort focused on better understanding the clinical course of Friedreich's ataxia and identifying potential clinical endpoints for future clinical trials. Once we and Neurocrine identify a lead candidate for this program, we plan to complete IND enabling studies to evaluate its safety and efficacy.

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. VY-SOD102, our clinical candidate for the treatment of a monogenic form of ALS, is composed of an AAV capsid and a proprietary transgene that harnesses the RNA interference pathway to selectively knock down, or reduce, levels of SOD1 mRNA. VY-SOD102 has the potential to durably reduce the levels of toxic mutant SOD1 protein in the spinal cord to slow the progression of disease. In late 2018 and early 2019, we presented data on VY-SOD102 administered with a novel delivery paradigm comprising a one-time infusion after laminectomy to the cervical region of the spinal cord. Preclinical data previously reported included significant reductions of SOD1 mRNA throughout the spinal cord of the Göttingen minipig, which has a spinal cord similar in length and diameter to the human spinal cord. This novel delivery approach with VY-SOD102 yielded well-tolerated and significant reduction of SOD1 mRNA throughout the spinal cord at four weeks post-dosing. In connection with the restructuring of our gene therapy relationship with Sanofi Genzyme, we decided to reallocate resources to our Huntington's disease program and new discovery efforts. We intend to seek a partner to advance our preclinical program for SOD1 ALS and no longer expect to file an IND application for our ALS program prior to partnering.

In 2018, we began collaborating with AbbVie 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. In early 2019, we presented on the use of therapeutic antibodies targeting various forms of tau to prevent, reduce, or slow the development of tau pathology as an important potential therapeutic strategy for Alzheimer's disease and other tauopathies. Because of the blood-brain barrier, or BBB, only very low levels of antibody distribute to the brain from the systemic circulation after passive immunization, resulting in modestly reduced tau pathology in animal models. Separately, in 2019, we began collaborating with AbbVie 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 and development against pathological species of alpha-synuclein for the potential treatment of Parkinson's disease and other synucleinopathies. Our vectorized antibody approach aims to circumvent this limitation by delivering, with a potential one-time intravenous, or IV, administration, the genes that encode for the production of therapeutic antibodies utilizing our novel BBB-penetrant AAV capsids. This approach could potentially result in higher levels of therapeutic antibodies in the brain compared with current systemic administration of antibodies.

Both of our collaborations with AbbVie were terminated by AbbVie, effective as of August 3, 2020, or the AbbVie Collaboration Termination Date. As a result of such terminations, we were relieved of future research and development obligations under each collaboration. Exclusivity provisions restricting either party or any of its respective affiliates from directly or indirectly exploiting any vectorized antibody compound targeting a tau protein or an alpha-synuclein protein and restricting us, alone or jointly with any third party, from directly or indirectly exploiting specified antibodies targeting a tau protein or contributed by AbbVie to the AbbVie Alpha-Synuclein Collaboration have also terminated. Each party retains a royalty-free, exclusive license to the other's interest in certain intellectual property rights developed by either party under the collaborations, or Joint IP, to exploit antibodies it contributed to each collaboration as well as royalty-free, non-exclusive licenses to Joint IP for any other purpose. Further, AbbVie has granted us, effective as of the AbbVie Collaboration Termination Date, in the case of the AbbVie Tau Collaboration, a worldwide, royalty-free, transferable, sublicensable (though multiple tiers), exclusive license to AbbVie's interest in Joint IP to exploit research compounds or product candidates that were investigated under the collaborations and do not encode antibodies contributed by AbbVie or include active pharmaceutical ingredients owned by AbbVie or its affiliates and, in the case of the AbbVie Alpha-Synuclein Collaboration, a worldwide, royalty-free, transferable, sublicensable (though multiple tiers), non-exclusive license to AbbVie's interest in Joint IP for any purpose, in each case for all human diagnostic, prophylactic and therapeutic uses. We are not obligated to repay the upfront payment we received from AbbVie in connection with entering into either collaboration agreement, but we are no longer eligible to receive option payments, milestone payments or royalties thereunder. We expect to continue to advance our research and development efforts related to vectorized antibodies, including 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 (i) a tau protein and (ii) pathological species of alpha-synuclein for the potential treatment of Parkinson's disease and other synucleinopathies, and we are currently evaluating our options for advancing these efforts individually or with other potential collaborators.

In addition to the programs described above, 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 and are also actively exploring additional potential treatment methods that can utilize an AAV vector. In early 2019, we presented on our discovery and development of novel AAV capsids that cross the BBB after IV administration with improved transduction of the brain and spinal cord and enhanced cellular specificity using libraries under the control of either the neuron-specific synapsin, or SYN, promoter or the astrocyte-specific glial fibrillary acidic protein, or GFAP, promoter to apply selective pressure for capsid variants that transduce the cell type of interest. As part of that effort, our scientists have developed a proprietary system called TRACER™ (Tropism Redirection of AAV by Cell Type-Specific Expression of RNA) to facilitate the selection of AAV capsids with BBB crossing and cell-specific transduction properties for particular therapeutic applications. The TRACER system is a broadly-applicable, functional RNA-based AAV capsid screening platform that allows for rapid *in vivo* evolution of AAV capsids with cell-specific transduction properties in wild-type animals. Multiple capsid variants have been identified with up to 1,000-fold improvement of central nervous system transduction in mouse models over AAV9 following IV administration after three rounds of selection. We are applying the TRACER system towards selecting AAV capsids with improved BBB-penetrant properties in the non-human primate.

Finally, we have developed our own real-time, intra-operative, MRI compatible device, the Variable Trajectory Array Guide, or V-TAG™, that can be used with other neuro-navigational systems for the administration of drugs and other surgical procedures, to avoid blood vessels and reduce the risk of potential hemorrhage during surgery, and to maximize drug coverage of the targeted structures. In July 2018, the Center for Devices and Radiological Health, or the CDRH, of the FDA provided 510(k) clearance for V-TAG. We are currently working with ClearPoint Neuro, Inc. (formerly known as MRI Interventions, Inc.), or CLPT, on process development and manufacturing of the device, and in March 2019, we transferred our premarket notification (510(k)) clearance for V-TAG to CLPT. Investigators have used an alternative MRI-compatible device called the ClearPoint® System in the Phase 1b clinical trial of VY-AADC (NBIb-1817) and Phase 1 posterior trajectory trial. We expect to use both V-TAG and the ClearPoint System in the RESTORE-1 Phase 2 clinical trial.

We have incurred significant operating losses since our inception. Our net losses were $32.9 million for the six months ended June 30, 2020. As of June 30, 2020, we had an accumulated deficit of $345.6 million. 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, as we:

- continue investing in our gene therapy platform to optimize capsid engineering and payload development, manufacturing, dosing, and delivery techniques;
- work with our collaboration partner Neurocrine to advance VY-AADC (NBIb-1817) as a treatment for Parkinson’s disease through Phase 1 clinical development and the VY-AADC (NBIb-1817) RESTORE-1 Phase 2 clinical trial;
- advance VY-HTT01 as a treatment for Huntington’s disease into a first-in-human clinical trial and a separate longitudinal observational study;
- initiate additional preclinical studies and clinical trials for, and continue research and development of, our other programs;
- conduct joint research and development under our strategic collaborations for the research, development, and commercialization of certain of our pipeline programs;
- 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;
- expand our manufacturing capabilities;
- develop, obtain and maintain regulatory clearances for devices to deliver our AAV gene therapies, and to provide financial and operating support to partners manufacturing and supplying these devices for use in our clinical development program;
- seek marketing and regulatory approvals for VY-AADC (NBIb-1817) or other product candidates or devices that arise from our programs that successfully complete clinical development;
- maintain, expand, protect and enforce 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, 2020, we recognized $3.5 million of collaboration revenue from the AbbVie Tau Collaboration, $4.3 million of collaboration revenue from the AbbVie Alpha-Synuclein Collaboration, and $38.9 million of collaboration revenue from the Neurocrine Collaboration.

For additional information about our revenue recognition policy related to collaborations and a description of the key terms of our collaboration arrangements with AbbVie and Neurocrine, refer to Note 8, *Commitments and Contingencies*, of our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q.

For the foreseeable future, we expect substantially all of our revenue will be generated from our existing collaboration agreement with Neurocrine and from any other strategic relationships we may enter into. If our development efforts are successful, we may also generate revenue from product sales in the future.

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, clinical and 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;
- continued acceptable safety profiles of the products following approval; and
- retention of 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 monitor the PD-1101 Phase 1b clinical trial and the PD-1102 Phase 1 trial and continue to enroll the RESTORE-1 Phase 2 clinical trial of VY-AADC (NBIb-1817) as a treatment for Parkinson’s disease, and move our other product candidates, including VY-HTT01 for the treatment of Huntington’s disease, into clinical trials. Additionally, we expect research and development costs associated with activities under our strategic collaborations to increase. 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 RESTORE-1 Phase 2 clinical trial of VY-AADC (NBIb-1817), the expanded efforts in connection with our strategic collaborations, and the ongoing research and development activities

and 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.

Other Income (Expense), net

Interest and other (expense) income consists primarily of interest income on our marketable debt securities and the gain or loss on the equity securities investment in CLPT.

Critical Accounting Policies and Estimates

We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as critical because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate. There were no changes to our critical accounting policies during the six months ended June 30, 2020 as compared to those identified in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019. It is important that the discussion of our operating results that follow be read in conjunction with the critical accounting policies disclosed in our Annual Report on Form 10-K, as filed with the SEC on March 3, 2020.

Recently Adopted Accounting Pronouncements

In 2016, the Financial Accounting Standards Board, or FASB, issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial* Instruments, or ASU 2016-13, which amends the impairment model by requiring entities to use a forward-looking approach based on expected losses to estimate credit losses on certain types of financial instruments, including trade receivables and available-for-sale debt securities. We adopted the standard on January 1, 2020. Based on the composition of our investment portfolio, current market conditions, and historical credit loss activity, the adoption of this standard did not have a material impact on our consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement*, or ASU 2018-13. This standard eliminates, adds and modifies certain disclosure requirements for fair value measurements as part of its disclosure framework project. We adopted the standard on the required effective date of January 1, 2020. The adoption of this standard did not have a material impact on our consolidated financial statements and related disclosures.

Results of Operations

Comparison of the three months ended June 30, 2020 and 2019

The following table summarizes our results of operations for the three months ended June 30, 2020 and 2019, together with the changes in those items in dollars:

	Three Months Ended June 30,		
	2020	2019	Change
	(in thousands)		
Collaboration revenue	$ 28,681	$ 46,087	$ (17,406)
Operating expenses:			
Research and development	29,423	28,576	847
General and administrative	8,239	8,322	(83)
Total operating expenses	37,662	36,898	764
Other income, net:			

Interest income	346	2,097	(1,751)
Other expense	(46)	(133)	87
Total other income, net	300	1,964	(1,664)
Net (loss) income	(8,681)	11,153	(19,834)

Collaboration Revenue

Collaboration revenue was $28.7 million and $46.1 million for the three months ended June 30, 2020 and 2019, respectively. During the three months ended June 30, 2020, collaboration revenue included $1.1 million related to research services from the AbbVie Tau Collaboration, $3.1 million related to research services from the AbbVie Alpha-Synuclein Collaboration, and $24.5 million related to research services and cost reimbursement from the Neurocrine Collaboration. During the three months ended June 30, 2019, collaboration revenue included $30.2 million related to the Sanofi Genzyme Collaboration, $3.2 million related to research services from the AbbVie Tau Collaboration, $0.2 million related to research services from the AbbVie Alpha-Synuclein Collaboration, and $12.5 million related to research services and cost reimbursement from the Neurocrine Collaboration.

The decrease in collaboration revenue in the three months ended June 30, 2020 was primarily due to amounts recorded as revenue as a result of the termination of the Sanofi Genzyme Collaboration in June 2019. As a result of the termination, we paid $10.0 million to Sanofi Genzyme and expect to pay an additional $10.0 million within fifteen days of the filing of an IND application for a Post-Termination HD Product, which we currently anticipate to occur before the end of 2020. We recognized $30.2 million of revenue related to the Sanofi Genzyme Collaboration in the three months ended June 30, 2019. The reduction in revenue was offset by a $12.8 million increase in revenue related to research services and cost reimbursements from the collaborations with Neurocrine and AbbVie.

Our collaboration revenues were not materially impacted by the coronavirus disease 2019, or COVID-19, pandemic during the three months ended June 30, 2020. In subsequent periods, the COVID-19 pandemic could affect our collaboration revenues and our operations. For example, if the temporary pause in screening for the RESTORE-1 Phase 2 clinical trial is extended as a result of factors related to the COVID-19 pandemic, VY-AADC Program collaboration revenues may decrease or be delayed, and the timeline for the VY-AADC Program could be extended.

As a result of the termination of the collaboration and option agreements with AbbVie in August 2020, we expect to recognize as revenue all remaining amounts included in deferred revenue related to these agreements in the second half of 2020.

Research and Development Expense

Research and development expense increased by $0.8 million from $28.6 million for the three months ended June 30, 2019, to $29.4 million for the three months ended June 30, 2020. The following table summarizes our research and development expense for the three months ended June 30, 2020 and 2019, together with the change in those items in dollars:

	Three Months Ended June 30,		
	2020	2019	Change
	(in thousands)		
External research and development expenses	$ 13,452	$ 14,094	$ (642)
Employee and consultant related expenses	11,365	10,007	1,358
Facility and other expenses	4,460	4,308	152
License fees	146	167	(21)
Total research and development expenses	$ 29,423	$ 28,576	$ 847

The increase in research and development expense for the three months ended June 30, 2020 was primarily attributable to the following:

- approximately $1.4 million for increased research and development employee-related and consultant compensation costs as we continue to increase research and development headcount to support our program pipeline; and

- approximately $0.2 million for 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 primarily related to clinical and manufacturing activities for the VY-AADC Program for Parkinson's disease, and preclinical and manufacturing activities for our VY-HTT01 Program for Huntington's disease

The COVID-19 pandemic continues to evolve rapidly. Our corporate headquarters is in Massachusetts, a state particularly hard hit by the pandemic. We have and will continue to adhere to applicable guidelines and safety measures including stay-at-home policies and the reporting of only essential personnel for business continuity to ensure the safety of our employees, consultants, contractors, and staff. Certain of our clinical trial sites and collaboration partners have experienced facility closures or been subject to quarantines, travel restrictions and other governmental restrictions and have appropriately diverted attention and resources to respond to the impacts of COVID-19 on their own operations and personnel. Some have even become involved in research and development efforts related to COVID-19.

The current workplace safety measures that we have enacted in response to COVID-19 have required a reduction in on-site activity at our facilities in Massachusetts, including in our laboratories in which preclinical experiments are conducted. As a result, we have had to prioritize our preclinical experiments and terminate or delay some non-critical experiments in order to maintain critical experiments for our preclinical programs.

We have experienced, and expect to continue to experience, a slower pace of enrollment in the RESTORE-1 Phase 2 clinical trial, and we and our collaboration partner Neurocrine have temporarily paused screening to allow participating clinical trial sites to evaluate the impact of the pandemic on the clinical trial including the implementation of recent protocol amendments and the safety of trial participants. We and Neurocrine expect patient screening to resume during the second half of 2020 at clinical sites in the RESTORE-1 trial.

We will continue to monitor the issues raised by the global spread of COVID-19 and have put in place and will continue to put in place measures as appropriate and necessary for, or that we believe to be in the best interest of, our business, employees, collaborators, stockholders, and the community.

We do not expect the termination of the collaboration agreements with AbbVie in August 2020 to result in a significant impact to research and development expenses.

General and Administrative Expense

General and administrative expense decreased by $0.1 million from $8.3 million for the three months ended June 30, 2019 to $8.2 million for the three months ended June 30, 2020. The decrease in general and administrative expense was primarily attributable to a decrease of approximately $0.1 professional fees to support the advancement of Voyager's pipeline programs.

Other Income, net

Interest and other income of approximately $0.3 million and $2.0 million was recognized during the three months ended June 30, 2020 and 2019, respectively, related to interest income on marketable securities balances, in addition to gains and losses on our common stock investment in and warrants to purchase shares of common stock of CLPT.

Comparison of the six months ended June 30, 2020 and 2019

The following table summarizes our results of operations for the six months ended June 30, 2020 and 2019, together with the changes in those items in dollars:

	Six Months Ended June 30,		
	2020	2019	Change
	(in thousands)		
Collaboration revenue	$ 46,748	$ 51,284	$ (4,536)
Operating expenses:			
Research and development	61,718	53,407	8,311
General and administrative	18,444	17,981	463
Total operating expenses	80,162	71,388	8,774
Other income, net:			
Interest income	1,324	3,242	(1,918)
Other (expense) income	(854)	845	(1,699)
Total other income, net	470	4,087	(3,617)
Net loss	$ (32,944)	$ (16,017)	$ (16,927)

Collaboration Revenue

Collaboration revenue was $46.7 million and $51.3 million for the six months ended June 30, 2020 and 2019, respectively. During the six months ended June 30, 2020, collaboration revenue included $3.5 million related to research services from the AbbVie Tau Collaboration, $4.3 million related to research services from the AbbVie Alpha-Synuclein Collaboration, and $38.9 million related to research services and cost reimbursement from the Neurocrine Collaboration. During the six months ended June 30, 2019, collaboration revenue included $31.6 million related to the Sanofi Genzyme Collaboration, $4.9 million related to research services from the AbbVie Tau Collaboration, $0.4 million related to research services from the AbbVie Alpha-Synuclein Collaboration, and $14.4 million related to research services and cost reimbursement from the Neurocrine Collaboration.

The decrease in collaboration revenue in the six months ended June 30, 2020 was primarily due to amounts recorded as revenue as a result of the termination of the Sanofi Genzyme Collaboration in June 2019. As a result of the termination, we paid $10.0 million to Sanofi Genzyme and expect to pay an additional $10.0 million within fifteen days of the filing of an IND application for a Post-Termination HD Product, which we currently anticipate to occur before the end of 2020. We recognized $31.6 million of revenue related to the Sanofi Genzyme Collaboration in the six months ended June 30, 2019. The reduction in revenue was partially offset by a $27.0 million increase in revenue related to research services and cost reimbursements from the collaborations with Neurocrine and AbbVie.

Research and Development Expense

Research and development expense increased by $8.3 million from $53.4 million for the six months ended June 30, 2019, to $61.7 million for the six months ended June 30, 2020. The following table summarizes our research

and development expense, for the six months ended June 30, 2020 and 2019, together with the changes in those items in dollars:

	Six Months Ended June 30,		
	2020	2019	Change
	(in thousands)		
External research and development expenses	$ 28,081	$ 27,542	$ 539
Employee and consultant related expenses	23,938	17,931	6,007
Facility and other expenses	9,402	7,616	1,786
License fees	297	318	(21)
Total research and development expenses	$ 61,718	$ 53,407	$ 8,311

The increase in research and development expense for the six months ended June 30, 2020 was primarily attributable to the following:

- approximately $6.0 million related to research and development employee and contractor compensation costs as we continue to increase research and development headcount to support our program activities;
- approximately $1.8 million for 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.
- approximately $0.5 million for increased external research and development costs primarily related to clinical and manufacturing activities for the VY-AADC Program for Parkinson's disease.

General and Administrative Expense

General and administrative expense increased by $0.4 million from $18.0 million for the six months ended June 30, 2019 to $18.4 million for the six months ended June 30, 2020. The increase in general and administrative expense was primarily attributable to the following:

- approximately $2.5 million for increased compensation costs associated with the increase in administrative function headcount;
- partially offset by a decrease of approximately $1.3 million in intellectual property related expenses and $0.7 million for legal costs resulting from the completion of our strategic collaborations from the prior year.

Other Income, net

Interest and other income of approximately $0.5 million and $4.1 million were recognized during the six months ended June 30, 2020 and 2019, respectively, related to interest income on marketable securities balances in addition to gains on our common stock investment in and warrants to purchase shares of common stock of CLPT.

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, the Sanofi Genzyme Collaboration which commenced in February 2015 and was terminated in June 2019, the AbbVie Tau Collaboration, which commenced in February 2018 and was terminated effective August 3, 2020, the AbbVie Alpha-Synuclein Collaboration, which commenced in February 2019 and was terminated effective August 3, 2020, and the Neurocrine Collaboration, which commenced in March 2019.

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. In connection with the Neurocrine Collaboration Agreement, Neurocrine also paid us $50.0 million as consideration for an equity purchase of 4,179,728 shares of our common stock in March 2019.

As of June 30, 2020, we had cash, cash equivalents, and marketable debt securities of $229.7 million.

Cash Flows

The following table provides information regarding our cash flows for the six months ended June 30, 2020 and 2019:

	Six Months Ended June 30,	
	2020	**2019**
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$ (49,999)	$ 93,605
Investing activities	107,155	(139,549)
Financing activities	2,167	78,970
Net increase in cash, cash equivalents, and restricted cash	$ 59,323	$ 33,026

Net Cash (Used in) Provided by Operating Activities

Net cash used in operating activities was $50.0 million during the six months ended June 30, 2020 compared to $93.6 million of cash provided by operating activities during the six months ended June 30, 2019. The increase in cash used in operating activities for the six months ended June 30, 2020 was primarily due to an increase in operating expenses and a decrease in deferred revenue. Cash provided by operating activities during the six months ended June 30, 2019 was primarily due to an increase in deferred revenue of $106.1 million from the upfront payments related to the AbbVie Alpha-Synuclein Collaboration and the Neurocrine Collaboration, partially offset by $16.0 million of net loss adjusted for non-cash items.

Net Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was $107.2 million during the six months ended June 30, 2020 compared to $139.5 million of cash used in investing activities during the six months ended June 30, 2019. The net cash provided by investing activities for the six months ended June 30, 2020 was primarily due to $125.5 million from maturities of marketable securities partially offset by $15.0 million for purchases of marketable securities and $3.4 million for purchases of property and equipment. Cash used in investing activities for the six months ended June 30, 2019 was primarily due to purchases of $314.4 million of marketable securities and $3.2 million for purchases of property and equipment, offset by $177.8 million of proceeds from maturities of marketable securities.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $2.2 million during the six months ended June 30, 2020, due to the proceeds from the exercise of stock options. Net cash provided by financing activities was $79.0 million during the six months ended June 30, 2019, primarily from the issuance of 4,179,728 shares to Neurocrine pursuant to a stock purchase agreement in connection with the Neurocrine Collaboration as well as proceeds from 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 and as we continue to enter into or expand efforts on our collaboration agreements. 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 increasing costs associated with operating as a public company, meeting financial controls, satisfying regulatory and quality standards, fulfilling healthcare compliance requirements, and maintaining product, clinical trial and directors' and officers' liability insurance coverage. 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 that our existing cash, cash equivalents, and marketable debt securities as well as amounts expected to be received for reimbursement of development costs from the Neurocrine Collaboration will enable us to meet our planned operating expenses and capital expenditure requirements into mid-2022. 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 our strategic collaborations, 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, including any intellectual property associated with such candidates or technologies, or acquire or invest in other businesses, such as our investment in ClearPoint Neuro, Inc. (formerly known as MRI Interventions, Inc.), or CLPT;
- the costs related to evaluating possible alternative devices that may be useful in the delivery of our product candidates, including our potential delivery devices, such as the Variable Trajectory Array Guide , or V-TAG™;
- the costs of advancing our manufacturing capabilities and securing manufacturing arrangements for pre-commercial and commercial production;

- the level of product sales by us or our collaborators from any product candidates for which we obtain marketing approval in the future;

- the costs of operating as a public company, meeting applicable financial, regulatory and quality control standards, fulfilling healthcare compliance requirements, and maintaining adequate product, clinical trial and directors' and officers' liability insurance coverage; 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 milestone payments 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. We do not have any committed external source of funds other than the amounts we are entitled to receive from our collaboration partners for reimbursement of research and development expenses, 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.

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, 2020:

	Total	Remaining 2020	1 to 3 Years	3 to 5 Years	More than 5 Years
			(in thousands)		
Operating lease commitments[1]	$ 42,850	$ 2,980	$ 12,461	$ 13,219	$ 14,190

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

In March 2020, we entered into an agreement to lease our 75 Hayden Avenue facility until October 29, 2030. The expected contractual obligation under this lease is approximately $25.6 million, to be paid over the ten year term of the lease. These payments are not included in the detailed table above.

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.

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, 2019, as filed with the SEC on March 3, 2020.

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; Smaller Reporting Company Status

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 of 1933, as amended, or 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.

EGCs are also permitted to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. Subject to certain conditions, as an EGC, we intend to rely on certain of these exemptions, including without limitation, (i) not being required to provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act; (ii) 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, known as the auditor discussion and analysis; (iii) reduced disclosure obligations regarding executive compensation; and (iv) exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. 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. As we became a public company in November 2015, we expect to lose our status as an EGC on January 1, 2021.

We are also a "smaller reporting company," as defined in Rule 12b-2 under the Exchange Act. We would cease to be a smaller reporting company if we have a non-affiliate public float in excess of $250 million and annual revenues of at least $100 million, or annual revenues less than $100 million and a non-affiliate public float in excess of $700 million, determined on an annual basis. Even after we no longer qualify as an EGC, we may still qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements. In addition to the above reduced disclosure requirements applicable to EGCs, as a smaller reporting company, we are permitted and intend to rely on certain exemptions from disclosure requirements that are applicable to other public companies that are not smaller reporting companies. These permitted exemptions include (i) being permitted to provide only two years of audited consolidated financial statements in our Annual Report on Form 10-K, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure; (ii) not being required to furnish a contractual obligations table in "Management's Discussion and Analysis of Financial Condition and Results of Operations"; and (iii) not being required to furnish a stock performance graph in our annual report to stockholders. As our revenues exceeded $100 million for the 2019 fiscal year, we expect to lose our status as a smaller reporting company in 2021 and to no longer qualify for the reduced disclosure requirements applicable to smaller reporting companies when our Annual Report on Form 10-K for the twelve months ended December 31, 2020 is issued.

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 notes. 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.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition, or results of operations during the three and six months ended June 30, 2020.

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, 2020. 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, 2020, 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, 2020, 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 any product candidates will fail to be safe and efficacious, 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 net losses were $32.9 million and $16.0 million for the six months ended June 30, 2020 and 2019, respectively. As of June 30, 2020, we had an accumulated deficit of $345.6 million.

We historically have financed our operations primarily through private placements of our redeemable convertible preferred stock, public offerings of our common stock, and strategic collaborations, including those with Sanofi Genzyme Corporation, or Sanofi Genzyme, AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company, or collectively, AbbVie, and Neurocrine Biosciences, Inc., or Neurocrine. 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, 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. On March 11, 2019, in connection with our collaboration with Neurocrine, we sold 4,179,728 shares of common stock to Neurocrine at a price of $11.9625 per share, resulting in net proceeds to us of $50.0 million.

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 strategic collaborations. We expect that it could be several years before we have a commercialized product, if we ever succeed in doing so. 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 capsid engineering and payload development, manufacturing, dosing, and delivery techniques;

- work with our collaboration partner Neurocrine to advance VY-AADC (NBIb-1817) as a treatment for Parkinson's disease through Phase 1 clinical development and the VY-AADC (NBIb-1817) RESTORE-1 Phase 2 clinical trial;
- advance VY-HTT01 as a treatment for Huntington's disease into a first-in-human clinical trial and a separate longitudinal observational study;
- initiate additional preclinical studies and clinical trials for, and continue research and development of, our other programs;
- conduct joint research and development under our strategic collaborations for the research, development, and commercialization of certain of our pipeline programs;
- 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;
- expand our manufacturing capabilities;
- develop, obtain and maintain regulatory clearances for devices to deliver our AAV gene therapies, and to provide financial and operating support to partners manufacturing and supplying these devices for use in our clinical development program;
- seek marketing and regulatory approvals for VY-AADC (NBIb-1817) or other product candidates or devices that arise from our programs that successfully complete clinical development;
- maintain, expand, protect and enforce 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 redesign or modify trials or studies or to perform trials or studies in addition to those currently expected;

- there are any delays in the 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, alone or with our collaborators, 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 collaboration 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 (NBIb-1817), which we have the option to co-commercialize with Neurocrine in the United States, is being evaluated in the Phase 1b clinical trial, the separate Phase 1 clinical trial, and the RESTORE-1 Phase 2 clinical trial. 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, 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 have the financial, operating and technical capabilities to provide adequate products and services, in both amount and quality, 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, enforcing 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 redesign or modify preclinical studies or clinical trials or to perform preclinical studies or 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, 2020, our cash, cash equivalents, and marketable debt securities were $229.7 million. Based upon our current operating plan, we expect that our existing cash, cash equivalents, and marketable debt securities, as well as ongoing reimbursement amounts expected from development costs related to our collaboration and license agreement with Neurocrine, or the Neurocrine Collaboration Agreement, will enable us to meet our planned operating expenses and capital expenditure requirements into mid-2022.

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 our strategic collaborations 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, including any intellectual property associated with such candidates or technologies, or acquire or invest in other businesses, such as our investment in CLPT;
- the costs related to evaluating possible alternative devices that may be useful in the delivery of our product candidates, including our potential delivery devices, such as V-TAG;
- the costs of advancing our manufacturing capabilities and securing manufacturing arrangements for pre-commercial and commercial production;
- the level of product sales by us or our collaborators from any product candidates for which we obtain marketing approval in the future;
- the costs of operating as a public company, meeting applicable financial, regulatory and quality control standards, fulfilling healthcare compliance requirements, and maintaining adequate product, clinical trial and directors' and officers' liability insurance coverage; 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 milestone payments 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.

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. 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. 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 a clinical stage company. Our operating history is short, and to date has 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 and potentially infeasible to predict the duration and cost of development of, and subsequently obtaining regulatory approval for, our product candidates. Only two AAV gene therapy products have been approved in the United States. In Europe, only two AAV gene therapy products have been approved.

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 (NBIb-1817), is in clinical development, and the remainder of our product candidates are in preclinical development. AAV gene therapies are a relatively new technology. 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 the preclinical testing or development of our product candidates and that such problems or delays will not cause unanticipated costs, or that any such problems or delays can be solved in a timely or profitable basis, if at all. 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 Luxturna, an AAV gene therapy product by Spark for patients with an inherited form of vision loss, and Zolgensma, an AAV gene therapy product by Avexis, a Novartis company, for pediatric patients with spinal muscular atrophy. The FDA has also approved two non-AAV gene therapy products, Kymriah by Novartis International AG, for pediatric and young adult patients with a form of acute lymphoblastic leukemia and Yescarta by Kite Pharma, Inc., for adult patients with certain forms of non-Hodgkin lymphoma. In Europe, two AAV gene therapy products, Glybera by uniQure N.V., or uniQure, and Luxturna by Spark, have been granted marketing authorization; however, uniQure decided not to pursue renewal of such authorization in 2017 and has since withdrawn Glybera from the European market. The European Commission also has approved four non-AAV gene therapy products, Strimvelis by Orchard Therapeutics (Netherlands) BV, Kymriah, Yescarta, and ZYNTEGLO by bluebird bio for a form of transfusion-dependent β-thalassemia.

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 review process, require us to modify current studies or perform additional studies or increase our development costs, which in turn 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.

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 PD-1101 Phase 1b clinical trial of VY-AADC (NBIb-1817), the PD-1102 Phase 1 trial exploring the delivery of VY-AADC (NBIb-1817) using a posterior trajectory, and the RESTORE-1 Phase 2 clinical trial are being conducted at multiple 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 protocols for the trials are amended, and any delay in or failure to obtain institutional IRB approval for any protocol or protocol amendment could delay, interrupt, or limit the conduct of the clinical trial at one or more participating clinical trial sites. For example, the recent amendments to the RESTORE-1 clinical trial protocol must be reviewed by institutional IRBs at participating clinical trial sites, and we and our collaboration partner

Neurocrine paused screening of new patients for enrollment in April 2020, in part to facilitate and assess IRB review of such updates.

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 European Union. 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. We have requested feedback from the FDA on, among other matters, the regulatory pathway for VY-AADC (NBIb-1817) and the design of our proposed pivotal program. We had multiple interactions with the FDA throughout 2018 and received certain written feedback requiring additional clarification. In December 2018, we held a Type B meeting with the FDA to discuss the overall development and pivotal program for VY-AADC (NBIb-1817). In connection with our Neurocrine Collaboration Agreement, we agreed to transfer sponsorship of the VY-AADC Program to Neurocrine, which required the related investigational new drug, or IND, application to be transferred to Neurocrine. The transition process required additional regulatory filings with and review by the FDA. We received written feedback from the FDA, including FDA guidance received during the Type B meeting that in a disease such as Parkinson's two adequate and well-controlled clinical trials is suggested. Based upon feedback received from the FDA, we and Neurocrine have amended the RESTORE-1 clinical trial protocol to support a future registration filing for VY-AADC (NBIb-1817) for the treatment of Parkinson's disease in the United States. The protocol amendments include increasing the planned enrollment to approximately 85 patients, from the previously planned 42 patients, and future enrollment in the trial will be randomized 2:1 to VY-AADC (NBIb-1817) or sham surgery, respectively, compared to the previous 1:1 randomization. Any further guidance that we may receive from the FDA could lead to further modification of the clinical VY-AADC (NBIb-1817) protocol and to additional costs or delays in the VY-AADC Program.

We plan to continue to seek and incorporate FDA guidance in our ongoing development plans for each of our potential clinical candidates. If we fail to consult or solicit guidance from regulators or are unable to obtain sufficiently frequent or detailed guidance from regulators, we may be required to delay or discontinue development of certain of our product candidates. Additional steps to receive guidance from regulators may result in a review and approval process that is longer than we otherwise would have expected. In addition, the FDA routinely grants pre-IND meetings with sponsors seeking to initiate clinical trials. We previously sought and received FDA feedback on the VY-HTT01 development program in a pre-IND meeting in 2017. Because the FDA only grants one pre-IND meeting per product in a given indication, we have not had formal additional consultations with the FDA concerning subsequent changes to the program. The FDA could request additional preclinical data or modifications to our VY-HTT01 development plan, and we may only be informed of such request after we file an IND. 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. Our product candidates may fail to show the desired safety and efficacy in preclinical testing or clinical development despite demonstrating promising results in earlier preclinical studies or clinical trials. In addition, the outcome of preclinical testing and early clinical trials may not be predictive of the success of later stage clinical trials. Similarly, interim results generated from clinical trials 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 the Phase 1b clinical trial and the separate Phase 1 clinical trial exploring the delivery of VY-AADC (NBIb-1817) using a posterior trajectory (PD-1101 and PD-1102, respectively), 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 sustained or 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.

There is a high failure rate for product candidates proceeding through preclinical studies and clinical trials. 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 dosing and coverage of the putamen in the VY-AADC (NBIb-1817) Phase 1b clinical trial, the separate Phase 1 clinical trial, and the RESTORE-1 Phase 2 clinical trial are different than the dosing and coverage of the putamen in prior clinical trials conducted by other parties. The maximum total vector genome dose chosen in the RESTORE-1 Phase 2 clinical trial may not demonstrate the safety and effectiveness of VY-AADC (NBIb-1817) in the RESTORE-1 Phase 2 clinical trial, or in the planned RESTORE-2 Phase 3 trial. Any failure to demonstrate safety or effectiveness could result in a decision to modify dosing and/or coverage of the putamen in any subsequent clinical trials, and such decisions could cause a delay in achieving marketing authorization, or may result in limiting or terminating the program entirely.

The clinical trial results of some of our collaborators have been negatively affected by factors that had not been fully anticipated prior to the design of the clinical trials. For example, the magnitude of some of the clinical responses seen in the Phase 1 clinical trial of AAV2-AADC, a therapy similar to VY-AADC (NBIb-1817) we previously evaluated in early-stage clinical trials, was similar to the placebo effects observed in previous surgical therapies for Parkinson's disease. As a result, we are unable to rely on the results of this prior Phase 1 trial as an indicator of the efficacy of treatment with VY-AADC (NBIb-1817). We and Neurocrine believe that to increase the likelihood of a clinical benefit, the dose and volume of infusion of VY-AADC (NBIb-1817) should be optimized to substantially increase the coverage of the putamen, the region of the brain targeted by VY-AADC (NBIb-1817). However, it is not possible at this time to know if we are optimizing these parameters, and as a result, to know if we will be able to achieve sufficient coverage of the putamen and a clinical benefit.

The PD-1101 Phase 1b clinical trial of VY-AADC (NBIb-1817) incorporated several design features in an attempt to increase the coverage area of the putamen, particularly the posterior putamen. We employed larger infusion volumes and higher doses of VY-AADC (NBIb-1817), and we used the ClearPoint® System to provide real-time, intra-operative, magnetic resonance imaging, or MRI, assistance to the physician surgically administering VY-AADC (NBIb-1817) to the patient.

In the PD-1102 Phase 1 clinical trial, we utilized posterior, or back of the head, delivery of VY-AADC (NBIb-1817) into the putamen, compared to a transfrontal, or top of the head, delivery approach used in the PD-1101 Phase 1b clinical trial described above. A posterior approach better aligns the infusion of VY-AADC (NBIb-1817) 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 (NBIb-1817) with this posterior approach has been well-tolerated to date with no reported serious adverse events, or SAEs.

Due to the nature of the techniques used in the Phase 1 clinical development and the numerous variables that can be changed, it is possible that the data generated from this trial may not provide evidence of statistically significant or durable 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 (NBIb-1817) that ultimately reaches the putamen, leading to highly variable results. Similarly, we have limited experience to date with the posterior delivery approach which we have selected as the preferred surgical route of administration for the RESTORE-1 Phase 2 clinical trial. The use of a posterior approach may not generate outcomes that are clinically superior to those achieved with a transfrontal approach.

For the RESTORE-1 Phase 2 clinical trial, we have selected a dose of up to 2.5×10^{12} vector genomes as a maximum total bilateral dose. This dosing level 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 dosing level in a clinical trial. To achieve safety, primary and secondary efficacy endpoints, the dose concentration and volume selected for the RESTORE-1 Phase 2 clinical trial may be modified, and regardless of the dose concentration and volume selected, we may never achieve desired safety and efficacy outcomes.

The RESTORE-1 Phase 2 trial is a randomized, double-blind, placebo-surgery controlled trial with a planned enrollment of approximately 85 patients who have been diagnosed with Parkinson’s disease for at least four years, are not responding adequately to oral medications, and have at least three hours of OFF time during the day as measured by a validated self-reported patient diary. Patients will be randomized 2:1 to VY-AADC (NBIb-1817) or sham surgery, respectively. Patient eligibility criteria and the protocol design, including the total number of patients in the trial and the number of patients who receive VY-AADC (NBIb-1817) or placebo, may change during the course of the trial in response to recruiting challenges, clinical patient assessments, data collection, statistical analysis modifications, and other factors, such as modifications to the clinical trial protocol made to date.

The primary efficacy endpoint of the RESTORE-1 Phase 2 clinical trial is the mean improvement from baseline to 12 months on time without troublesome dyskinesia, or good ON time, as measured by a validated self-reported patient diary at 12 months compared to placebo. Secondary endpoints include diary OFF time, other motor function and quality of life measures from the Unified Parkinson’s Disease Rating Scales (UPDRS-II,-III scores), the Parkinson’s Disease Questionnaire (PDQ-39), and patient’s global function as measured by the proportion of participants with improvement on the Clinical Global Impression (CGI) score. The trial will also measure non-motor symptoms from the Non-Motor Symptom Scale (NMSS), as well as safety. Primary and secondary endpoints may be adjusted during the trial in response to changes in the protocol design.

Biomarker data collected during the RESTORE-1 Phase 2 clinical trial will include measurements of the coverage of the putamen, the specific region of the brain targeted with VY-AADC (NBIb-1817), and measurements of AADC enzyme expression and activity in the putamen measured by positron emission tomography (PET) using fluorodopa F-18. Changes in patients’ daily doses of oral levodopa and related medications will also be recorded.

We plan to continue to seek and incorporate FDA guidance in our clinical trial plans. We are currently evaluating the written feedback from the FDA, including guidance from the Type B meeting to conduct two adequate and well-controlled clinical trials for a large patient population such as Parkinson’s disease. Additional interaction with the FDA regarding the RESTORE-1 and RESTORE-2 clinical trial plans could result in changes to the current plan.

Additionally, we are using a different manufacturing process for our AAV gene therapy vector in the RESTORE-1 Phase 2 clinical trial and the planned RESTORE-2 Phase 3 clinical trial. We have begun to manufacture VY-AADC (NBIb-1817) using our baculovirus/Sf9 system as opposed to manufacturing in HEK 293 cells, which were used in the 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 the RESTORE-1 Phase 2 clinical trial and the planned RESTORE-2 Phase 3 clinical trial in Parkinson's disease may differ from the results of the Phase 1b (PD-1101) or the separate Phase 1 clinical trial (PD-1102) based on the use of VY-AADC (NBIb-1817) manufactured using our baculovirus/Sf9 system as opposed to using HEK 293 cells.

We may in the future conduct, and intend to 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 may include international sites in the RESTORE-1 Phase 2 clinical trial. The transfer of sponsorship of the VY-AADC Program to Neurocrine requires Neurocrine to be the sponsor of the RESTORE-1 Phase 2 clinical trial in any international sites. Any sponsorship transition could require additional regulatory filings with and review by regulatory officials, and may lead to additional costs or delays in the initiation of the RESTORE-1 Phase 2 clinical trial and the enrollment of patients in those international sites.

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, economic, environmental, and health risks relevant to specific foreign countries, including risks related to natural disasters or disease outbreaks, including the current coronavirus disease 2019, or COVID-19, pandemic.

We may encounter substantial delays or difficulties in commencement, enrollment or completion of our preclinical studies or clinical trials, or 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. To conduct clinical trials, we must first complete preclinical testing and studies to support IND applications or similar applications in other jurisdictions. We cannot be certain of the timely completion or successful outcome of our preclinical testing and studies and cannot predict if the FDA or similar regulatory authorities outside the United States will accept our planned clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our preclinical and clinical programs.

We have very limited experience with clinical trials. The transfer of sponsorship of the VY-AADC Program to Neurocrine requires Neurocrine to be the sponsor of the RESTORE-1 Phase 2 clinical trial in any sites. Any sponsorship transition could require additional regulatory filings with and review by the FDA, European Union, or other regulatory officials, and may lead to additional costs or delays in the initiation of the RESTORE-1 Phase 2 clinical trial in those sites.

The RESTORE-1 Phase 2 clinical trial of VY-AADC (NBIb-1817) is being conducted at several locations. 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 the RESTORE-1 Phase 2 clinical trial for VY-AADC (NBIb-1817) 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 trial 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. Additionally, we and our collaboration partner Neurocrine recently temporarily paused the screening of candidates for the RESTORE-1 clinical trial, in part to assess the impact of the COVID-19 pandemic on the safety of study participants and on the implementation of recent amendments to the clinical trial protocol.

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 (NBIb-1817);
- formulation changes to our product candidates, which 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 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 (NBIb-1817) RESTORE-1 Phase 2 and RESTORE-2 Phase 3 clinical trials as we have historically used, and expect to use, the ClearPoint System, which is only available at a small number of academic medical centers in the United States;
- the ability to commercially launch V-TAG, 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 in some or all localities, 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 or collaborators on trial design, implementation, or management;
- 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 IRBs 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, our collaboration partners, any CROs we engage, or any other third parties to adhere to clinical trial protocols or regulatory requirements;
- failure by us, our collaboration partners, any CROs we engage, or any other third parties to perform in accordance with the FDA’s good clinical practices, or GCPs, 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 the RESTORE-1 Phase 2 clinical trial in Parkinson’s disease associated with the commercial availability of V-TAG;

- 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 and potential delays to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. In addition, if we make manufacturing or formulation changes to our product candidates, such as our previous transition from an HEK 293-based production system to a baculovirus/Sf9 AAV production system, 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 SAEs associated with our product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates, if we are able to do so 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 otherwise become party to dispute proceedings; 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 (NBIb-1817) and VY-HTT01 are designed to 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 (NBIb-1817). In the RESTORE-1 Phase 2 clinical trial of VY-AADC (NBIb-1817), we are using the ClearPoint System to provide accurate placement of the cannula in the putamen and allow for real-time, intra-operative MRI to assist the physician in visualizing the delivery of VY-AADC (NBIb-1817) 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. The ClearPoint System has only been used in limited gene therapy neurosurgeries to date. One patient in the Phase 1b trial experienced two 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 (NBIb-1817). In the Phase 2 and future trials, we may use V-TAG, a proprietary real-time, intra-operative, MRI-compatible device that we developed with CLPT. For VY-SOD102 in the treatment for amyotrophic lateral sclerosis, or ALS, the product candidate is planned to be injected directly into the spinal cord. Limited clinical data are available for this route of administration. If other side effects were to occur in connection with the surgical procedures described above, or problems were encountered with the use of the ClearPoint System or V-TAG, 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 expression of a gene or the production of 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. For products for which we may obtain orphan drug designation or exclusivity, we may be unable to prevent the approval or marketing authorization of other similar products based upon regulator decisions regarding product "sameness".

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 (NBIb-1817) 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 criterion 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 (NBIb-1817) 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 applicable regulatory authority 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 six 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 (NBIb-1817) for Parkinson's disease. On March 15, 2019, we received notification from the FDA that VY-HTT01, an AAV gene therapy containing a transgene that encodes a microRNA targeting huntingtin messenger RNA, had been granted orphan drug designation for the treatment of Huntington'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 other drug or biological product is not the "same drug" or biological product or is clinically superior in that it is shown to be safer or more effective or makes a major contribution to patient care. In particular, the concept of what constitutes the "same drug" for purposes of orphan drug exclusivity remains in flux in the context of gene therapies, and the FDA has issued recent draft guidance suggesting that it would not consider two gene therapy products to be different drugs solely based on minor differences in the transgenes or vectors. 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 or prevent other products from receiving marketing authorization due to decisions of the applicable regulatory agency regarding "sameness" of the products.

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 have sought and may in the future 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 have sought and may in the future 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 the VY-AADC (NBIb-1817) gene therapy treatment for advanced Parkinson's disease with motor fluctuations that are refractory to medical management. The designation was based on data from the 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 a product candidate that received RMAT designation no longer meets the conditions for designation. Alternatively, we or our collaborative partners may decide not to proceed with the clinical development of a product candidate that has previously received RMAT designation or decide to pursue such product candidate for an indication for which it has not received RMAT 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 (NBIb-1817) 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 a product candidate's 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 current or future collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they may not be able to commercialize our products, and our ability to generate revenue may 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 CROs 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, in or the enactment of additional statutes or regulations, or 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 current or future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Additionally, in July 2018, we received 510(k) regulatory clearance of V-TAG, our potential delivery device, from the Center for Devices and Radiological Health of the FDA, or CDRH. 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 expect to rely on third parties in the development and manufacture of our potential delivery devices. In May 2018, for example, we entered into a master services and supply agreement with CLPT which provides for CLPT 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 V-TAG. In March 2019, we transferred our premarket notification (510(k)) clearance for the V-TAG device to CLPT. CLPT has sole responsibility for regulatory compliance related to V-TAG.

Accordingly, if we or any current or future collaborators experience delays in obtaining approval or if we or they fail to obtain or retain approval of our product candidates and devices, the commercial prospects for our product candidates may be harmed and our ability to generate revenues could 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 current good manufacturing practice, or 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 such regulatory authority disagrees with the promotion, marketing or labeling of that product, the 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 collaboration 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 biopharmaceutical industry is characterized by intense and dynamic competition to develop new technologies and proprietary therapies. Any product candidates that we successfully develop into products and commercialize may compete with existing therapies and new therapies that may become available in the future. While we believe that our gene therapy platform, product programs, product candidates and scientific expertise in the fields of gene therapy and neuroscience provide us with competitive advantages, we face potential competition from various sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, governmental agencies and public and private research institutions.

We are aware of several companies focused on developing AAV gene therapies in various indications, including AAVANTIBio, Inc., Abeona Therapeutics, Inc., Adverum Biotechnologies, Inc., Aevitas Therapeutics, Inc., Apic Bio, Inc., Applied Genetic Technologies Corporation, Asklepios BioPharmaceutical, Inc., Audentes Therapeutics, Inc., AveXis, Inc. (acquired by Novartis AG in 2018), or AveXis, Axovant Sciences Ltd., or Axovant, Biogen, Inc., or Biogen, Brain Neurotherapy Bio, Inc., GenSight Biologics SA, Homology Medicines, Inc., LogicBio Therapeutics, Inc., Lysogene SA, MeiraGTx Ltd., or MeiraGTx, Neurogene, Inc., Passage Bio, Inc., Pfizer, Inc., Prevail Therapeutics, Inc., PTC Therapeutics, Inc., REGENXBio Inc., Sarepta Therapeutics, Inc., Solid Biosciences, Inc., Spark Therapeutics, Inc. (acquired by F. Hoffmann-La Roche Ltd., or Roche, in 2019), or Spark, StrideBio, Inc., and uniQure NV, or uniQure, 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 (NBIb-1817) will compete with a variety of therapies currently marketed and in development for Parkinson’s disease, including DBS marketed by Medtronic plc, Abbott Laboratories (acquired from St. Jude Medical in 2017), and other medical device companies, DUOPA/Duodopa marketed by AbbVie, as well as other novel, non-oral forms of levodopa in development, including Mitsubishi Tanabe Pharma’s ND0612 (acquired from

NeuroDerm in 2017), Acorda Therapeutics' inhaled levodopa, INBRIJA (CVT-301), and Sunovion Pharmaceuticals', or Sunovion's, sublingual apomorphine, APL-130277. Gene therapy competition for Parkinson's disease previously included AMT-090 or AAV-GDNF, but this was deprioritized by uniQure in 2016. Axovant is developing a second generation LentiVector gene therapy, AXO-Lenti-PD (previously OXB-102, licensed from Oxford Biomedica in 2018). MeiraGTx is developing AAV-GAD, acquired from Vector Neurosciences, Inc. in 2018.

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

- VY-HTT01 for Huntington's disease will potentially compete with RG6042 (IONIS-HTTR$_x$) being developed by Roche in collaboration with Ionis Pharmaceuticals, Inc., or Ionis, WVE-120101 and WVE-120102 being developed by WAVE Life Sciences Ltd. in collaboration with Takeda Pharmaceutical Company Limited, or Takeda, a Zinc Finger Protein (ZFP) therapy being developed by Sangamo Therapeutics, Inc. in collaboration with Shire plc, and gene therapies being developed by uniQure and Spark;

- VY-SOD102 for a monogenic form of ALS will potentially compete with BIIB067 (IONIS-SOD1R$_x$) being developed by Biogen, in collaboration with Ionis, and gene therapies being developed by AveXis and Apic Bio, Inc.;VY-FXN01 for Friedreich's ataxia will potentially compete with AAV gene therapies being developed by Pfizer, Inc., PTC Therapeutics, Inc., StrideBio, Inc. in collaboration with Takeda, AAVANTIBio, Inc., and AveXis;

- Our Tau program for tauopathies including Alzheimer's disease, progressive supranuclear palsy, and frontotemporal dementia will potentially compete with tau antibodies being developed by Roche Genentech Inc. in collaboration with AC Immune SA, Eli Lilly & Co., AbbVie, Biogen, and several other companies, as well as an antisense oligonucleotide program being developed by Ionis in collaboration with Biogen; and

- Our alpha-synuclein program for synucleinopathies, including Parkinson's disease, Lewy Body Dementia, and multiple system atrophy, will potentially compete with alpha-synuclein antibodies being developed by Roche in collaboration with Prothena Corporation, Biogen in collaboration with Neurimmune AG, AstraZeneca plc in collaboration with Takeda, and several other companies, as well as an antisense oligonucleotide program being developed by Ionis in collaboration with Biogen.

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 V-TAG. Investigators in the Phase 1b, the separate Phase 1 posterior trajectory trial, and the RESTORE-1 Phase 2 clinical trial of VY-AADC (NBIb-1817) have used and are using the ClearPoint System from CLPT.

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, including recent transactions involving a number of gene therapy companies, 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 or reducing the number of available subjects for enrollment in our clinical trials to support regulatory submissions and approvals of our product. 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 or manufacturing control requirements. In many countries outside the United States, a product candidate must be separately 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. 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. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the United Kingdom will not accept high regulatory alignment with the European Union.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us 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, AbbVie, and Neurocrine. If any ongoing or future collaboration agreements were to be terminated, our business financial condition, results of operations and prospects could 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 the Parkinson's disease program, or VY-AADC Program, Friedreich's ataxia program, or FA Program, and Huntington's disease program, or Huntington's Program, and a future program, collectively, the Split Territory Programs, with an incremental option to co-commercialize the product candidate from our Huntington's Program in the United States and (ii) worldwide rights to our spinal muscular atrophy program. If Sanofi Genzyme would have exercised an option for a Split Territory Program, except for the VY-AADC Program, it would have been required to make an option exercise payment to us. 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, as well as tiered royalty payments based on a percentage of net sales of product candidates from the programs for which Sanofi Genzyme exercised its option.

In June 2019, we and Sanofi Genzyme executed a termination agreement to terminate the Sanofi Genzyme Collaboration Agreement, or the Sanofi Genzyme Termination Agreement. Under the terms of the Sanofi Genzyme Termination Agreement, Sanofi Genzyme relinquished its rights to its exclusive license options to the Huntington's Program, FA Program and the unnamed future program described above, and we were relieved of our obligations to perform the research and development services under those programs under the Sanofi Genzyme Collaboration Agreement. As a result, we gained worldwide rights to the Huntington's Program and ex-U.S. rights to the FA Program. Our ex-U.S. rights to the FA Program were, in turn, transferred from us to Neurocrine Biosciences pursuant to the Neurocrine Collaboration Agreement. In connection with the Sanofi Genzyme Termination Agreement, we also relinquished our rights to the spinal muscular atrophy program. As of the termination date, we also waived our right to approximately $0.4 million in unused in-kind services, and we no longer had the right to receive any option payments, regulatory or commercial milestone payments or royalties from Sanofi Genzyme under the Sanofi Genzyme Collaboration Agreement.

In February 2018, we entered into an exclusive collaboration and option agreement with AbbVie, which we refer to as the AbbVie Tau 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 Tau Collaboration Agreement, we received an upfront payment of $69.0 million and were eligible to receive option exercise payments, future development and regulatory milestone payments and royalties prior to the termination of the AbbVie Tau Collaboration Agreement, effective August 3, 2020. Following such termination, we are evaluating our options for potentially advancing our tau program in the future. If we seek another collaboration partner for the program, we may be unable to find a suitable collaborator on a timely basis, on terms acceptable to us, or at all. If we opt to progress this program ourselves, our expenditures would increase, and we might lack the resources or expertise that an appropriate collaboration partner could provide. If we are unable to find a suitable collaboration partner or unable or unwilling to increase our financial commitment to the tau program to undertake its development, we may have to delay or curtail the program.

In January 2019, we entered into the Neurocrine Collaboration Agreement for the research, development and commercialization of four programs including the VY-AADC Program, our FA Program, and two programs to be determined by us and Neurocrine at a later date, or the Discovery Programs. Under the terms of the agreement, we received an upfront payment of $115.0 million and may receive future development and regulatory milestones and royalties. In connection with the Neurocrine Collaboration Agreement, Neurocrine also paid us $50.0 million as consideration for an equity purchase of 4,179,728 shares of our common stock. In June 2019, in conjunction with the termination of the Sanofi Genzyme Collaboration Agreement, we and Neurocrine amended the Neurocrine Collaboration Agreement to facilitate the transfer of the ex-U.S. rights to the FA Program which we acquired from Sanofi Genzyme to Neurocrine. In connection with the amendment, we received a $5.0 million payment from Neurocrine.

Under the terms of the Neurocrine Collaboration Agreement, subject to the rights retained by us thereunder, we have agreed to collaborate with Neurocrine on, and to grant, exclusive, royalty-bearing, non-transferable, sublicensable licenses to certain of our intellectual property rights for all human and veterinary diagnostic, prophylactic, and therapeutic uses for the research, development, and commercialization of gene therapy products, which we refer to as the Collaboration Products, under (i) the VY-AADC Program, on a worldwide basis; (ii) the FA Program, on a worldwide basis; and (iii) each Discovery Program, on a worldwide basis. We refer to each of these programs as a Neurocrine Program and, collectively, as the Neurocrine Programs.

Pursuant to development plans to be agreed upon by the parties, which will be overseen by a joint steering committee, we have operational responsibility, subject to certain exceptions, for the conduct of each Neurocrine Program (prior to specified transition events for each program), and are required to use commercially reasonable efforts to develop the Collaboration Products. Neurocrine has agreed to be responsible for all costs incurred by us in conducting these activities for each Neurocrine Program in accordance with an agreed budget. If we breach our development responsibilities or in certain circumstances upon a change in control of us, Neurocrine has the right but not the obligation to assume the activities under such Neurocrine Program.

Upon the occurrence of specified events for each program, Neurocrine has agreed to assume responsibility for development, manufacturing and commercialization activities for such program and to pay us milestones and royalties on future net sales. For each of the VY-AADC Program and the FA Program, we have the option to co-develop and co-commercialize such program upon the occurrence of a specified event. Should we elect to exercise our co-development and co-commercialization option, we and Neurocrine have agreed to enter into a cost- and profit-sharing arrangement whereby we and Neurocrine agree to jointly develop and commercialize Collaboration Products for such program and share in its costs, profits and losses, and we forfeit certain milestones and royalties on net sales in the United States during the effective period of the applicable co-development and co-commercialization agreement. As described above, our research and development activities in connection with a collaboration might not be successful. Neurocrine may terminate the Neurocrine Collaboration Agreement in its entirety or on a program-by-program or country-by-country basis by providing at least 180-day advance notice if such notice is provided prior to the first commercial sale of the Collaboration Product to which the termination applies or one-year advance notice if such notice is provided after the first commercial sale of the Collaboration Product to which the termination applies. If Neurocrine were to terminate the agreement, we would become responsible for all research and development expenses relating to the Neurocrine Programs, and would not receive any future milestone payments or royalty payments under the Neurocrine Collaboration Agreement.

Neurocrine might not be successful in obtaining approvals for the product candidates arising from our collaboration, or commercializing or manufacturing the resulting products. Further, Neurocrine’s objectives in connection with the collaboration may not be consistent with our best interests. With respect to the rights granted to Neurocrine by us, Neurocrine could take actions that may be 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.

In February 2019, we entered into a collaboration agreement, which we refer to as the AbbVie Alpha-Synuclein Collaboration Agreement, for the research, development, and commercialization of AAV gene therapy products directed against alpha-synuclein for indications including Parkinson’s disease and other synucleinopathies. Under the terms of the AbbVie Alpha-Synuclein Collaboration Agreement, we received an upfront payment of $65.0 million and were eligible to receive option exercise payments, future development and regulatory milestone payments and royalties prior to the termination of the AbbVie Alpha-Synuclein Collaboration Agreement, effective August 3, 2020. Following such termination, we are evaluating our options for potentially advancing our alpha-synuclein program in the future. If we seek another collaboration partner for the program, we may be unable to find a suitable collaborator on a timely basis, on terms acceptable to us, or at all. If we opt to progress this program ourselves, our expenditures would increase, and we might lack the resources or expertise that an appropriate collaboration partner could provide. If we are unable to find a suitable collaboration partner or unable or unwilling to increase our financial commitment to the alpha-synuclein program to undertake its development, we may have to delay or curtail the program.

We have only used the ClearPoint System to deliver our product candidates to date. 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 (NBIb-1817) 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 (NBIb-1817) to the putamen using real-time, intra-operative, magnetic resonance imaging, or MRI, scans 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, the separate Phase 1 posterior trajectory trial, and the RESTORE-1 Phase 2 clinical trial for VY-AADC (NBIb-1817) have used and are using the real-time, intra-operative, MRI imaging system known as the ClearPoint System. The ClearPoint System is manufactured by CLPT. Not all neurosurgical units within the United States utilize the ClearPoint system and may employ other neuro-navigational systems that are not compatible with real-time MRI imaging. We and Neurocrine intend to use the ClearPoint System at certain sites in the RESTORE-1 Phase 2 clinical trial and may choose to use it in future clinical trials of VY-AADC (NBIb-1817) 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 issues with CLPT, 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 (NBIb-1817), as there currently is no other manufacturer of the ClearPoint System. Outside the United States, the ClearPoint System is not widely available or utilized in neurosurgical units.

We have developed V-TAG as our own real-time, intra-operative device that is compatible with MRI imaging and can be used with other neuro-navigational systems to dose VY-AADC (NBIb-1817) and for other surgical procedures. We believe that the experience we have gained from delivering VY-AADC (NBIb-1817) in our clinical trials to date and our work to develop V-TAG may inform AAV gene therapy delivery for our Huntington's Program and other projects. In July 2018, we received 510(k) regulatory clearance of V-TAG from the CDRH. 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 expect to rely on third parties in the development and manufacture of our potential delivery devices. In May 2018, we entered into a master services and supply agreement with CLPT for the development and manufacture of devices, including V-TAG. This agreement provides for CLPT to perform certain manufacturing, supply, development and other services, including the supply of the ClearPoint System and cannula devices. In March 2019, we transferred our premarket notification (510(k)) clearance for the V-TAG device to CLPT, and will work with CLPT on the manufacturing and clinical supply of the device.

As of December 31, 2019, CLPT reported cash and cash equivalents of $5.7 million and junior secured debt totaling approximately $2.1 million, and also reported a net loss of $5.5 million for the three months ended December 31, 2019. Management of CLPT historically expressed concerns about its ability to continue as a going concern. In January 2020, CLPT announced that it had completed a $17.5 million financing with PTC Therapeutics, Inc. and Petrichor Opportunities Fund I LP. CLPT's management has advised that its cash and cash equivalents balance as of December 31, 2019, when supplemented by the proceeds from this financing, are sufficient to support CLPT's operations for at least the next twelve months, however, there is risk that CLPT may fail to maintain sufficient funding to continue its operations and meet its obligations under our agreement with CLPT on a long-term basis. If CLPT, or any potential successor to CLPT, is not able to meet its obligations under our agreement with CLPT, and if we are not able to make suitable alternative arrangements for the supply of the ClearPoint System or V-TAG, the use of the ClearPoint System and V-TAG in our clinical trials could be adversely affected, and our clinical trials, including the RESTORE-1 Phase 2 clinical trial, could be delayed. In such circumstance, our business, financial condition, results of operations and prospects could be materially harmed.

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 may 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 might 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 current or future collaborators 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 or desired;
- 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 or expenses 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 preclinical studies and clinical trials, and if these third parties perform in an unsatisfactory manner, our business could be harmed.

We expect to rely on CROs, clinical trial sites, and other vendors to ensure our preclinical studies and clinical trials are conducted properly and on time. We may also engage third parties such as clinical data management organizations, medical institutions and clinical investigators to conduct or assist in our clinical trials or other preclinical and clinical research and development work. While we will have agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our third-party service providers' activities. Nevertheless, we will be responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal, quality, regulatory and scientific standards. Our reliance on these third parties does not relieve us of our regulatory responsibilities. For example, the Phase 1b clinical trial of VY-AADC (NBIb-1817) and the separate Phase 1 trial exploring the delivery of VY-AADC (NBIb-1817) using a posterior trajectory were conducted at several locations. We expect to conduct the RESTORE-1 Phase 2 clinical trial at over twenty 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. If we elect to internalize some or all activities related to the conduct of our preclinical studies or clinical trials that are currently performed by our third-party service providers, or if we are required to do so due to a service provider's termination of our relationship, then we may be required to source additional technology and personnel in order to perform the relevant activities. We may be unsuccessful in our efforts to internalize some or all relevant activities, either on the desired timeline or at all.

We and our third-party service providers are required to comply with the FDA's good laboratory practices, or GLPs, and GCPs for conducting, recording and reporting the results of IND-enabling preclinical 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 GLPs and GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites, and laboratories at which the FDA may determine that our preclinical studies and clinical trials did not comply with GLPs or GCPs. If we, our collaborators, or our third-party service providers fail to comply with applicable GLPs or GCPs, the preclinical or clinical data generated in our future preclinical studies or clinical trials may be deemed unreliable and the FDA may require us to perform additional preclinical studies or clinical trials before approving the relevant INDs or 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, our collaborators, 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 preclinical studies or 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, attention, expertise and resources to our clinical and nonclinical programs. These third-party service providers may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If our third-party service providers do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our preclinical studies or clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates could be harmed, our costs could increase, and our ability to generate revenues could be delayed.

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

We presently contract with third parties for the manufacturing of our program materials. We are currently assessing our manufacturing capabilities and although we do not currently have our own clinical or commercial scale manufacturing, we may choose to build those 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 by 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. Several of these raw materials, cells, and reagents are provided by a limited number of suppliers. Even though we aim to have backup supplies and suppliers 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 on our manufacturing processes, including 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 processes and facilities, or disruptions in such manufacturing processes, 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 a product candidate 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, our collaborators, or us could harm our business, financial condition, results of operations and prospects.

If our third-party manufacturers, our collaborators, 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, 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 or product candidates, 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 and our product delivery devices 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 and delivery devices, 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 and delivery devices must be stored and transported at temperatures within a certain range and in sterile environments. If these temperature and environmental conditions deviate, the remaining shelf-life of a product candidate or utility of a device could be impaired or its efficacy and safety could be negatively impacted, making it 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.

Failure to obtain access to or to protect intellectual property related to the manufacturing of our products or product candidates may result in changes, delays and/or inability to manufacture such products or product candidates.

The intellectual property related to the manufacture of biological products is complex. If we are unable to maintain control of manufacturing technology such as our trade secrets, or we are unable to protect ongoing improvements comprehensively and in a sufficient number of jurisdictions, it would impact our ability to produce products for commercial sale or product candidates for preclinical testing or clinical trials and our development timelines and operations timelines could be adversely affected.

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 (NBIb-1817) 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 G. Andre Turenne, our President and Chief Executive Officer. 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, collaborators, 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 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 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 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, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the TCJA, which was signed by President Trump 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, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated “Cadillac” tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.” The Congress may consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the Trump administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the

individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. On April 27, 2020, the U.S. Supreme Court reversed this decision.

In addition, the Centers for Medicare & Medicaid, or CMS, has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre-authorization, or PA, and step therapy, or ST, for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of “negotiated prices” while adding a definition of “price concession” into the regulations. It is unclear whether these proposed changes we be accepted, and if so, what effect such changes will have on our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued that such payments were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration has recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court’s ruling. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA and our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

In addition, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court’s ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. On December 18, 2019, that court affirmed the lower court’s ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Trump administration issued a plan to lower drug prices. Under this blueprint for action, the Trump administration indicated that

the Department of Health and Human Services will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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 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 the implementation of 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 Trump 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 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 European Union, including personal health data, is subject to the European Union 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 European Union, 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 has been and will continue to be a rigorous and time-intensive process that has increased and will continue to increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we or our collaborators may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities, which could adversely affect our business, prospects, financial condition and results of operations.

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 $1.0 million per occurrence and $2.0 million in the aggregate, and clinical testing liability insurance in the amount of $10.0 million per occurrence and $10.0 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 or from any other work-related injuries, 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.

A widespread outbreak of an illness or other health issue could significantly disrupt our operations. The current coronavirus disease 2019 (COVID-19) pandemic and the response to it have had, and we expect they will continue to have, an adverse effect on our business, operations, and future results.

Health issues such as epidemics or other medical emergencies outside of our control could significantly disrupt our operations and negatively impact our business.

In December 2019, a novel strain of coronavirus called severe acute respiratory syndrome coronavirus 2, also referred to as SARS-CoV-2, which causes the coronavirus disease 2019, also referred to as COVID-19, began to be reported in China and other countries. As of July 1, 2020, that outbreak has led to more than ten million confirmed cases worldwide, with many countries throughout the world confirming cases. The World Health Organization has declared the outbreak a pandemic and a global public health emergency. In addition to those who have been directly affected, millions more have been affected by local and national government efforts in the United States, the European Union and around the world to slow the spread of the pandemic through quarantines, travel restrictions, heightened border scrutiny and other measures.

The COVID-19 pandemic continues to evolve rapidly. Our corporate headquarters is in Massachusetts, a state particularly hard hit by the pandemic. We have and will continue to adhere to applicable guidelines and safety measures including stay-at-home policies and the reporting of only essential personnel for business continuity to ensure the safety of our employees, consultants, contractors, and staff. Certain of our clinical trial sites and collaboration partners have experienced facility closures or been subject to quarantines, travel restrictions and other governmental restrictions and have appropriately diverted attention and resources to respond to the impacts of COVID-19 on their own operations and personnel. Some have even become involved in research and development efforts related to COVID-19.

The current workplace safety measures that we have enacted in response to COVID-19 have required a reduction in on-site activity at our facilities in Massachusetts, including in our laboratories in which preclinical experiments are conducted. As a result, we have had to prioritize our preclinical experiments and terminate or delay some non-critical experiments in order to maintain critical experiments for our preclinical programs. If these measures must be maintained for an extended period of time, or if more restrictive workplace safety measures are recommended by federal and state authorities, we may need to delay or terminate other preclinical experiments, including critical experiments for our preclinical programs, which we expect could have a material adverse impact on our development and regulatory plans and timelines for our preclinical programs. To the extent that any preclinical experiments impacted in this manner relate to a collaboration program, our reimbursement revenues from collaborators for the relevant activities may decrease or be delayed.

We have experienced, and expect to continue to experience, a slower pace of enrollment in the RESTORE-1 Phase 2 clinical trial, and we and our collaboration partner Neurocrine have temporarily paused screening to allow participating clinical trial sites to evaluate the impact of the pandemic on the clinical trial including the implementation of recent protocol amendments and the safety of trial participants. It is possible that the institutional IRBs at one or more participating clinical trial sites will prioritize the review of research proposals related to COVID-19, which could delay or limit our ability to implement the recent protocol amendments at one or more sites. If such delays continue, our clinical supply of VY-AADC (NBIb-1817) might not be utilized prior to its expiration and could need to be replaced; our reimbursement revenues from Neurocrine related to VY-AADC (NBIb-1817) may decrease or be delayed; and the results from the RESTORE-1 Phase 2 clinical trial may also be delayed, any one of which we expect would have a material adverse impact on our development and regulatory plans and timelines for VY-AADC (NBIb-1817). We and Neurocrine plan to initiate the RESTORE-2 Phase 3 global registrational clinical study of VY-AADC (NBIb-1817) in Parkinson's disease during the first half of 2021.

The extent to which COVID-19 ultimately impacts our business, financial condition, and results of operations will depend on future developments such as the duration and scope of the pandemic and the response of policymakers, businesses and individuals that are highly uncertain and cannot be accurately predicted. In the future, there may be other material adverse impacts on our business and operations during the pandemic and once it subsides. Employees and other key personnel could become ill, quarantined, or otherwise unable to work and/or travel due to health reasons or governmental restrictions. Disruptions in the supply chain for personal protective equipment and other supplies critical for laboratory operations and/or the maintenance of current or future workplace safety measures could limit our ability to maintain business continuity. Regulators could be delayed in inspections, reviews, and approvals of product candidates including INDs and BLAs. Quarantines and travel restrictions could impact the ability of our third-party manufacturers and other suppliers to deliver clinical supplies or raw materials to us in a timely manner. Restrictions imposed on the construction industry could cause delays in completing our current and contemplated construction projects, resulting in program delays, cost increases and disruption to our current laboratory activities and general operations. Prolonged stay-at-home policies and a distributed workforce could inhibit our ability to restore operations to pre-COVID-19 pandemic norms and to attract, retain, and motivate qualified personnel, and consequently, to allow our operations to develop as anticipated and to make our expected organizational growth more difficult. We are dedicating financial resources towards mitigating operational adjustments arising from the COVID-19 pandemic. If we need to access the capital markets to address requirements arising from the impacts of COVID-19 pandemic, there is no assurance that financing will be available on attractive terms, if at all.

We will continue to monitor the issues raised by the global spread of COVID-19 and have put in place and will continue to put in place measures as appropriate and necessary for, or that we believe to be in the best interest of, our business, employees, collaborators, stockholders, and the community. However, there is no assurance that the pandemic will not have a material adverse impact on our business, operations, and future results.

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 cyber-attacks, computer viruses, unauthorized access, sabotage, 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 or the operations of those third parties with which we contract, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, and could require a substantial expenditure of resources to remedy. For example, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. We could also be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in our information systems and networks, including personal information of our employees. Outside parties may attempt to penetrate our systems or those of the third parties with which we contract or to fraudulently induce our employees or employees of such third parties to disclose sensitive information to gain access to our data.

The number and complexity of these threats continue to increase over time. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Despite our efforts, the possibility of these events occurring cannot be eliminated entirely. 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. 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 and the market perception of the effectiveness of our security measures could be harmed, our credibility could be damaged, and the further development and commercialization of our product candidates could be delayed.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Recent changes in tax law may adversely affect our business or financial condition. On December 22, 2017, President Trump signed into law the TCJA, which significantly revised the Internal Revenue Code of 1986, as amended. The TCJA, among other things, contained significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, or NOLs, which was enacted as part of the TCJA. It also provides that NOLs arising in any taxable year beginning after December 31, 2017, and before January 1, 2021, are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30 to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act or the CARES Act.

We might not be able to utilize a significant portion of our net operating loss carryforwards.

As of December 31, 2019, we had both federal and state net operating loss carryforwards of $175.2 million and $179.2 million, respectively, which expire beginning in 2033. These net operating loss carryforwards could expire unused and be unavailable to offset our future income tax liabilities. As described above under the heading "Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the TCJA, as amended by the CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. Nor is it clear how various states will respond to the TCJA, the FFCR Act or the CARES Act. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

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 Securities and Exchange Commission, or 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 such data 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. Additionally, because some patients with the diseases we are targeting in the United States, the European Union, and elsewhere may have increased susceptibility to COVID-19, the COVID-19 pandemic could limit the number of patients willing to participate in clinical trials related to our products or amenable to treatment with our products, 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.

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 the Neurocrine Collaboration Agreement, Neurocrine will fund the clinical development through the readout of the RESTORE-1 Phase 2 clinical trial for VY-AADC (NBIb-1817). After the data readout of the RESTORE-1 Phase 2 trial, we have the option to either: (1) co-commercialize VY-AADC (NBIb-1817) with Neurocrine in the United

States under a 50/50 cost- and profit-sharing arrangement and receive milestones and royalties based on ex-U.S. sales, or (2) retain the right to receive milestone payments and royalties based on global sales pursuant to the full global commercial rights granted to Neurocrine. Under the terms of the Neurocrine Collaboration Agreement for the FA Program, Neurocrine will fund the development through the Phase 1 clinical trial of VY-FXN01. After the data readout of the Phase 1 trial, we have the option to either: (1) co-commercialize VY-FXN01 with Neurocrine in the United States under a 60/40 cost- and profit-sharing arrangement, or (2) retain the right to receive milestone payments and royalties based on global sales pursuant to the full global commercial rights granted to Neurocrine.

In the future, we may seek to 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 receive 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, and to receive the support of medical associations and technology assessment committees. 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 are 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. 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 support and acceptance of medical associations and technology assessment committees, 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 few gene therapy products approved to date in the United States and the European Union. 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. Medical events such as the COVID-19 pandemic that emphasize harmful effects of certain viruses could also indirectly foster negative public perception of virus-based therapies. 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. SAEs 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 United Kingdom or 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; natural disasters including earthquakes, typhoons, floods and fires; or from social, 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 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 SEC 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. Certain of our license agreements contain "no challenge" clauses which preclude and prevent us from taking any action to limit or narrow the intellectual property of a licensor. In some cases, these limitations extend to any intellectual property of our licensor and not just that which is licensed to us. Such constraints may limit our ability to develop or commercialize products or to expand such efforts beyond the scope of any license. 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 any of our agreements involving intellectual property 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. Termination may also result in unfavorable terms associated with such termination or may result in obligations on our part to license or grant back intellectual property rights to prior licensors.

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 in some or all relevant jurisdictions 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. In some cases, we may be able to obtain patent protection, but such protections may expire before we commercialize the product protected by those rights, leaving us no meaningful protection for our products. In other cases, where our intellectual property is being managed by a third-party collaborator, licensee or partner, that third party may fail to act diligently in prosecuting, maintaining, defending or enforcing our patents. Such conduct may result in the failure to maintain or obtain protections, loss of

rights, loss of patent term or, in cases where a third party has acted negligently or inequitably, patents being found unenforceable.

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, narrow the scope, or eliminate the enforceability 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 behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, only upon issuance or 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.

In spite of a legal presumption of validity, the issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity, or enforceability which 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, any 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 or technical 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, and may compromise the strength of other intellectual property in our portfolio. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business.

On February 1, 2019 the government of Venezuela, in response to certain U.S. sanctions, began to require that foreign entities pay all official fees, including patent fees (either for pending matters or new petitions), in PETRO, a "cryptocurrency" created by the Nicolás Maduro administration in February 2018 as a way to collect U.S. dollars while avoiding American financial sanctions issued under an Executive Order of President Trump on March 19, 2018. The Executive Order banned transactions involving "any digital currency, digital coin, or digital token, that was issued by, for, or on behalf of the Government of Venezuela on or after January 9, 2018." The prohibition is applicable to any U.S. entity unless exempted by license. We do not hold such a license and therefore may not be able to secure patents in Venezuela.

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. With Brexit, there is uncertainty associated with obtaining, defending, and enforcing intellectual property rights in the United Kingdom. International treaties and regulations promulgated as a result of this transition could impede or eliminate our ability to obtain or maintain meaningful intellectual property rights in the United Kingdom. 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 technology or 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 our technology or one of our product candidates, the defendant could counterclaim that the patent covering such technology or 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 technology or 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 or our supporting technology. 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 directors, employees, consultants, and 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 these individuals 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, consultants, advisors 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.

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, became effective on March 16, 2013. The Leahy-Smith Act has resulted in an increased investment in filing applications earlier, and consequently has increased the uncertainties and costs surrounding the

prosecution of our patent applications, and may increase the enforcement or defense of our issued patents, all of which could harm our business, financial condition, results of operations and prospects.

The administrative tribunal created by the Leahy-Smith Act, known as the Patent Trial and Appeals Board, or PTAB, may have an impact on the operation of our business in the future. For example, 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 as the courts address issues such as patenting genes or gene products. The most recent guidance provided under *Berkheimer v HP, Inc*. (April 19, 2018) and *Vanda Pharmaceuticals, Inc. v West-Ward Pharmaceuticals* (June 7, 2018) instruct USPTO examiners on the ramifications of the court rulings as applied 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 court decisions referenced above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact decisions from the Supreme Court's decisions in *Mayo Collaborative Services v. Prometheus Laboratories* and *Molecular Pathology v. Myriad Genetics, Inc.* or other applicable court decisions 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 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. The ambiguities and changing law in all countries as to patenting genetic material may directly affect our ability to secure and/or maintain patent protection for our products.

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.

The Biologics Price Competition and Innovation Act of 2009 provides up to 12 years of market exclusivity for a reference biological product. We may not be able to obtain such exclusivity for our products. 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 European Community trademark registrations for the marks “V-TAG” and “VOYAGER TRAJECTORY ARRAY GUIDE.” We also own pending trademark applications in the USPTO for the marks “V-TAG”, V-TAG Logo, and “TRACER”. 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 own, license or may access 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 inventions, 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.

We may not be able to maintain sufficient control over our proprietary know-how or trade secrets when employees, consultants, advisors or persons with access to our proprietary information terminate their relationship with us.

Despite our efforts to protect our proprietary know-how and trade secrets, our competitors may discover this information, or obtain the benefit of this information, through a breach of confidentiality and/or non-competition obligations by persons who were formerly associated with us but who have established relationships as employees, contractors, consultants or advisors with other companies, including our competitors. If discovered in a timely manner, our efforts to enforce rights to protect against these types of breaches may not be possible under law, or may not be successful if commenced.

It is also possible that, as we grow and establish ourselves in multiple geographic areas, alignment and/or compliance with company polices may not be consistently maintained. In any such cases, the risk of loss of control or proper management of our proprietary information could jeopardize our intellectual property.

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.

Changes to national patent laws and diminished or limited access to United States and/or foreign patent counsel and the courts in response to the ongoing COVID-19 pandemic may compromise our ability to pursue, obtain, enforce or defend our intellectual property patent protections throughout the world.

In response to the ongoing COVID-19 pandemic, many national patent offices promulgated emergency measures and alternative procedures for filing, prosecuting and adjudicating disputes regarding intellectual property. While some of these new rules involve the provision of extensions for certain filing deadlines, none of these emergency-situation rules have been tested in a litigation setting or for their harmonization with the laws of other countries.

Access to the United States Patent Office and other patent offices has been restricted by government mandated shelter-in-place or stay-home orders thereby limiting our ability to appear before any tribunal in support of our intellectual property. Should the remaining electronic access to these tribunals be interrupted or non-existent, we may not be able to secure, defend or enforce patent protections in all jurisdictions.

We also rely on United States and foreign patent counsel in the management of our intellectual property. Should our access to counsel be diminished or lost due to effects of COVID-19 on these service providers and their organizations, we may not be able to manage, maintain or secure our intellectual property position.

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, LLC and Neurocrine represent beneficial ownership, in the aggregate, of approximately 36% of our outstanding common stock as of June 30, 2020. 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 restricted stock units, or RSUs, 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. We have also filed a registration statement on Form S-8 permitting shares of common stock issued on exercise of options or the settlement of RSUs 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. We also have an effective registration statement on Form S-3 for the sale of up to $300.0 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, of which we have reserved $100.0 million for the offering, issuance, and sale of common stock through at-the-market offerings or negotiated transactions under a sales agreement we entered into with Cowen and Company, LLC, on November 6, 2019.

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, 2020 through June 30, 2020, the sales price of our common stock ranged from a high of $14.62 to a low of $7.81 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, including the ability or willingness of our collaboration partners to fulfill their obligations to us;
- 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 a "smaller reporting company" and the reduced disclosure requirements applicable to such 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. As we became a public company in November 2015, we expect to lose our status as an EGC on January 1, 2021. We expect to continue to take advantage of some, but not all, of the available exemptions until such date.

Even after we no longer qualify as an emerging growth company, we might still qualify as a smaller reporting company, or SRC, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation. As our revenues exceeded $100 million for the 2019 fiscal year, we expect to lose our status as a smaller reporting company in 2021 and to no longer qualify for the reduced disclosure requirements applicable to smaller reporting companies when our Annual Report on Form 10-K for the twelve months ended December 31, 2020 is issued.

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

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.

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

As a public company, and particularly after we are no longer an EGC or SRC, we 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, or at all, 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 is inapplicable to actions arising under the Securities Exchange Act of 1934, as amended, and we likewise do not intend to apply this choice of forum provision to actions arising under the Securities Act of 1933, as amended.

This choice of forum provision may limit a stockholder's ability to bring a claim that is not arising under the Securities Exchange Act of 1934, as amended, or the Securities Act of 1933, as amended, 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 and business interruption that 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 6. EXHIBITS

The exhibits filed or furnished as part of this Quarterly Report 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
31.1	Certification of Principal Executive Officer pursuant to Exchange Act Rules 13a-14 or 15d-14.					X
31.2	Certification of Principal 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	Inline XBRL Instance Document. - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.					X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					

+ 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 10, 2020

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
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 31.1

Certification

I, G. Andre Turenne, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the period ended June 30, 2020 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 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 10, 2020

/s/ G. Andre Turenne

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

Exhibit 31.2

Certification

I, Allison Dorval, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the period ended June 30, 2020 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 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 10, 2020

/s/ Allison Dorval

Allison Dorval
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of Voyager Therapeutics, Inc. (the "Company") for the period ended June 30, 2020, 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 10, 2020

/s/ G. Andre Turenne

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

Date: August 10, 2020

/s/ Allison Dorval

Allison Dorval
Chief Financial Officer
(Principal Financial and Accounting Officer)