

---

**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, 2022**

**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)

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

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

**02139**  
(Zip Code)

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

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

---

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

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

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

The number of outstanding shares of the registrant's common stock, par value \$0.001 per share, as of August 1, 2022 was 38,647,592.

---

---

## 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 and our proprietary antibodies;
- our ability to continue to develop our proprietary gene therapy platform technologies, including our TRACER™ discovery platform, our vectorized antibody platform, and our proprietary antibodies;
- our ability to identify and optimize product candidates and proprietary AAV capsids;
- our strategic collaboration with and funding from our collaboration partner Neurocrine Biosciences, Inc., or Neurocrine, and from our licensing arrangements with Pfizer Inc., or Pfizer, and Novartis Pharma AG, or Novartis;
- our ongoing and planned preclinical development efforts, related timelines and studies;
- the timing of and our ability to submit applications and obtain and maintain regulatory approvals for our product candidates, including the ability to file investigational new drug, or IND, applications for our programs;
- our estimates regarding expenses, future revenues, capital requirements, and needs for additional financing;
- our ability to conduct clinical trials compliant with current good clinical practices and to develop a manufacturing capability compliant with current good manufacturing practices for our product candidates;
- 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 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 enter into future collaborations, strategic alliances, or licensing arrangements;

- our ability to control costs and reprioritize our product candidate pipeline successfully in connection with our strategic initiatives; and
- the potential impact of the COVID-19 pandemic on our research and development efforts 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 our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 8, 2022, particularly in “Part I, Item 1A — Risk Factors,” 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.

### **RISK FACTOR SUMMARY**

Investment in our securities involves risk and uncertainties that you should be aware of when evaluating our business. The following is a summary of what we believe to be the principal risks facing our business, as more fully described under “Part II, Item 1A—Risk Factors” and elsewhere in this Quarterly Report on Form 10-Q. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations.

- We have a history of incurring significant losses and anticipate that we will continue to incur losses for the foreseeable future and may never achieve or maintain consistent profitability. We may not be able to generate sufficient revenue from the commercialization of our product candidates and may never be consistently profitable.
- 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.
- To date, all of our revenue has been derived from our prior collaborations with Sanofi Genzyme Corporation, AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company, our ongoing collaboration with Neurocrine, and from our licensing arrangements with Pfizer Inc., or Pfizer, and Novartis Pharma AG, or Novartis. If any ongoing or future collaboration or licensing agreements were to be terminated, our business financial condition, results of operations and prospects could be harmed.
- Our AAV gene therapy and antibody product candidates are based on a proprietary technology and, in several disease areas, unvalidated treatment approaches, 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.
- 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.

- We are early in our development efforts. Our primary product candidates are in the discovery and preclinical development stages. 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.
- 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.
- 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.
- Our gene therapies 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.
- 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.
- If we are unable to obtain and maintain patent protection for our products and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our products and technology may be adversely affected.
- Our future success depends on our ability to retain key members of our management and research and development teams, and to attract, retain and motivate qualified personnel. Our inability to recruit, or the 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.
- A widespread outbreak of an illness or other health issue could significantly disrupt our operations. The current 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.

**VOYAGER THERAPEUTICS, INC.**

**FORM 10-Q**

**TABLE OF CONTENTS**

	Page
<u>PART I. FINANCIAL INFORMATION</u>	
<u>ITEM 1. CONDENSED CONSOLIDATED FINANCIAL STATEMENTS (UNAUDITED)</u>	6
<u>CONDENSED CONSOLIDATED BALANCE SHEETS</u>	6
<u>CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS</u>	7
<u>CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY</u>	8
<u>CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS</u>	9
<u>NOTES TO UNAUDITED CONDENSED CONSOLIDATED FINANCIAL STATEMENTS</u>	10
<u>ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS</u>	28
<u>ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK</u>	45
<u>ITEM 4. CONTROLS AND PROCEDURES</u>	46
<u>PART II. OTHER INFORMATION</u>	
<u>ITEM 1. LEGAL PROCEEDINGS</u>	46
<u>ITEM 1A. RISK FACTORS</u>	46
<u>ITEM 6. EXHIBITS</u>	113
<u>SIGNATURES</u>	114

**PART I. FINANCIAL INFORMATION**

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

	<u>June 30,</u> <u>2022</u>	<u>December 31,</u> <u>2021</u>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 78,329	\$ 117,433
Marketable securities, current	69,727	15,106
Related party collaboration receivable	151	732
Prepaid expenses and other current assets	3,421	3,427
Total current assets	<u>151,628</u>	<u>136,698</u>
Property and equipment, net	19,071	21,920
Deposits and other non-current assets	1,515	1,779
Operating lease, right-of-use asset	16,391	33,458
Total assets	<u>\$ 188,605</u>	<u>\$ 193,855</u>
<b>Liabilities and stockholders' equity</b>		
Current liabilities:		
Accounts payable	\$ 1,218	\$ 574
Accrued expenses	7,185	10,950
Other current liabilities	2,526	5,571
Deferred revenue, current	87,003	33,886
Total current liabilities	<u>97,932</u>	<u>50,981</u>
Deferred revenue, non-current	7,880	8,210
Other non-current liabilities	22,741	39,609
Total liabilities	<u>128,553</u>	<u>98,800</u>
Commitments and contingencies (see note 8)		
Stockholders' equity:		
Preferred stock \$0.001 par value: 5,000,000 shares authorized at June 30, 2022 and December 31, 2021; no shares issued and outstanding at June 30, 2022 and December 31, 2021	—	—
Common stock, \$0.001 par value: 120,000,000 shares authorized at June 30, 2022 and December 31, 2021; 38,439,251 and 37,918,395 shares issued and outstanding at June 30, 2022 and December 31, 2021, respectively	38	38
Additional paid-in capital	447,888	442,259
Accumulated other comprehensive loss	(364)	(138)
Accumulated deficit	(387,510)	(347,104)
Total stockholders' equity	<u>60,052</u>	<u>95,055</u>
Total liabilities and stockholders' equity	<u>\$ 188,605</u>	<u>\$ 193,855</u>

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

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

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2022	2021	2022	2021
Collaboration revenue	\$ 712	\$ 1,357	\$ 1,371	\$ 7,858
Operating expenses:				
Research and development	12,527	19,505	26,876	41,851
General and administrative	7,552	10,437	15,211	20,181
Total operating expenses	<u>20,079</u>	<u>29,942</u>	<u>42,087</u>	<u>62,032</u>
Operating loss	(19,367)	(28,585)	(40,716)	(54,174)
Other income (expense) :				
Interest income	219	48	271	132
Other (expense) income	61	(1,583)	39	2,273
Total other income (expense), net	<u>280</u>	<u>(1,535)</u>	<u>310</u>	<u>2,405</u>
Net loss	<u>\$ (19,087)</u>	<u>\$ (30,120)</u>	<u>\$ (40,406)</u>	<u>\$ (51,769)</u>
Other comprehensive (loss) income				
Net unrealized (loss) gain on available-for-sale securities	(141)	(3)	(226)	8
Total other comprehensive (loss) income	<u>(141)</u>	<u>(3)</u>	<u>(226)</u>	<u>8</u>
Comprehensive loss	<u>\$ (19,228)</u>	<u>\$ (30,123)</u>	<u>\$ (40,632)</u>	<u>\$ (51,761)</u>
Net loss per share, basic and diluted	<u>\$ (0.50)</u>	<u>\$ (0.80)</u>	<u>\$ (1.06)</u>	<u>\$ (1.38)</u>
Weighted-average common shares outstanding, basic and diluted	<u>38,298,426</u>	<u>37,581,381</u>	<u>38,183,192</u>	<u>37,543,387</u>

*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	Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Stockholders' Equity
<b>Balance at December 31, 2020</b>	37,368,027	\$ 37	\$ 430,324	\$ (134)	\$ (275,907)	\$ 154,320
Exercises of vested stock options	3,811	1	27	—	—	28
Vesting of restricted stock units	184,217	—	—	—	—	—
Stock-based compensation expense	—	—	3,498	—	—	3,498
Unrealized gain on available-for-sale securities, net of tax	—	—	—	11	—	11
Net loss	—	—	—	—	(21,649)	(21,649)
<b>Balance at March 31, 2021</b>	37,556,055	\$ 38	\$ 433,849	\$ (123)	\$ (297,556)	\$ 136,208
Vesting of restricted stock units	114,412	—	—	—	—	—
Issuance of common stock under ESPP	101,752	—	580	—	—	580
Stock-based compensation expense	—	—	3,871	—	—	3,871
Unrealized loss on available-for-sale securities, net of tax	—	—	—	(3)	—	(3)
Net loss	—	—	—	—	(30,120)	(30,120)
<b>Balance at June 30, 2021</b>	37,772,219	\$ 38	\$ 438,300	\$ (126)	\$ (327,676)	\$ 110,536
<b>Balance at December 31, 2021</b>	37,918,395	\$ 38	\$ 442,259	\$ (138)	\$ (347,104)	\$ 95,055
Exercises of vested stock options	11,484	—	12	—	—	12
Vesting of restricted stock units	312,090	—	—	—	—	—
Stock-based compensation expense	—	—	2,268	—	—	2,268
Unrealized loss on available-for-sale securities, net of tax	—	—	—	(85)	—	(85)
Net loss	—	—	—	—	(21,319)	(21,319)
<b>Balance at March 31, 2022</b>	38,241,969	\$ 38	\$ 444,539	\$ (223)	\$ (368,423)	\$ 75,931
Exercises of vested stock options	63,012	—	575	—	—	575
Vesting of restricted stock units	32,165	—	—	—	—	—
Issuance of common stock under ESPP	102,105	—	313	—	—	313
Stock-based compensation expense	—	—	2,460	—	—	2,460
Unrealized loss on available-for-sale securities, net of tax	—	—	—	(141)	—	(141)
Net loss	—	—	—	—	(19,087)	(19,087)
<b>Balance at June 30, 2022</b>	38,439,251	\$ 38	\$ 447,888	\$ (364)	\$ (387,510)	\$ 60,052

*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)*

	<b>Six Months Ended</b>	
	<b>June 30,</b>	
	<b>2022</b>	<b>2021</b>
<b>Cash flow from operating activities</b>		
Net loss	\$ (40,406)	\$ (51,769)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	4,809	7,592
Depreciation	4,016	2,459
Amortization of premiums and discounts on marketable securities	2	213
Other non-cash items	(2,469)	(2,460)
Changes in operating assets and liabilities:		
Related party collaboration receivable	581	6,254
Prepaid expenses and other current assets	6	893
Operating lease, right-of-use asset	2,556	1,922
Other non-current assets	—	69
Accounts payable	644	156
Accrued expenses	(3,652)	(3,357)
Operating lease liabilities	(2,647)	(1,891)
Other non-current liabilities	(287)	—
Deferred revenue	52,787	(4,092)
Net cash provided by (used in) operating activities	<u>15,941</u>	<u>(44,011)</u>
<b>Cash flow from investing activities</b>		
Purchases of property and equipment	(1,280)	(602)
Purchases of marketable securities	(54,848)	—
Proceeds from sales and maturities of marketable securities	—	57,632
Net cash (used in) provided by investing activities	<u>(56,128)</u>	<u>57,030</u>
<b>Cash flow from financing activities</b>		
Proceeds from the exercise of stock options	587	28
Proceeds from the purchase of common stock under ESPP	232	357
Net cash provided by financing activities	<u>819</u>	<u>385</u>
Net (decrease) increase in cash, cash equivalents, and restricted cash	(39,368)	13,404
Cash, cash equivalents, and restricted cash beginning of period	119,212	106,219
Cash, cash equivalents, and restricted cash end of period	<u>\$ 79,844</u>	<u>\$ 119,623</u>
<b>Supplemental disclosure of cash and non-cash activities</b>		
Capital expenditures incurred but not yet paid	\$ 113	\$ 111

*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 gene therapy and neuroscience company developing life-changing treatments and next-generation adeno-associated virus (“AAV”) capsids. The Company focuses on diseases where it believes a single dose AAV gene therapy or an antibody can either halt or slow disease progression or reduce symptom severity, therefore providing clinically meaningful impact to patients. The Company’s gene therapy platforms enable it to engineer, optimize, manufacture and deliver its AAV-based gene therapies that it believes have the potential to safely provide durable efficacy. The Company’s team of experts in the field of AAV gene therapy and neuroscience first identifies and selects diseases in which the Company believes an AAV gene therapy or an antibody will answer a high unmet medical need, be supported by target validation, offer an efficient path to human proof of biology, present robust preclinical pharmacology, and offer strong commercial potential. The Company then engineers and optimizes either an AAV vector for delivery of the virus payload to the targeted tissue or cells or a passive antibody for systemic delivery.

The Company is identifying proprietary AAV capsids, the outer viral protein shells that enclose genetic material of a virus payload. The Company’s team has developed a proprietary AAV capsid discovery platform called TRACER™ (Tropism Redirection of AAV by Cell Type-Specific Expression of RNA) to facilitate the selection of AAV capsids with blood brain barrier (“BBB”) crossing and cell-specific transduction properties for particular therapeutic applications. The TRACER discovery platform is a broadly applicable, functional RNA-based AAV capsid discovery platform that allows for rapid *in vivo* evolution of AAV capsids with cell-specific transduction properties in multiple species, including non-human primates. The Company believes its single dose gene therapies have the potential to be delivered with targeted or systemic surgical delivery or infusions, in conjunction with capsids it discovers through its TRACER platform (“TRACER capsids”).

The Company is also applying the TRACER discovery platform to identify capsid variant libraries and facilitate the selection of capsids with tropism and transduction in additional cell and tissue types. The Company is actively engaged in discussions with multiple parties to make TRACER capsids available to third parties for use in their drug development programs through potential licensing and other arrangements.

In addition to the Company’s TRACER discovery platform, the Company has developed a vectorized antibody platform which the Company believes will overcome many of the challenges of passive immunization. However, the Company has also seen promising preclinical results from the passive immunization approach and the Company is investigating both passive immunization and vectorized approaches to administer proprietary antibodies that selectively target pathological tau to address tauopathies.

The Company’s business strategy focuses on discovering, developing, manufacturing and commercializing its gene therapy and antibody programs. As part of this strategy, the Company has developed core competencies specific to AAV gene therapy and antibody development and manufacturing. This business strategy also includes business development activities that may include in-licensing activities or partnering certain programs in specific geographies with collaborators, as the Company has demonstrated through its ongoing collaboration with Neurocrine Biosciences, Inc. (“Neurocrine”) under a collaboration agreement that became effective in January 2019 (the “Neurocrine Collaboration Agreement”), or out-licensing activities including license agreements related to the TRACER capsids such as the Company’s October 2021 licensing agreement with Pfizer Inc. (“Pfizer”) and the Company’s March 2022 licensing agreement with Novartis Pharma AG (“Novartis”). The Company believes there is an ongoing opportunity for out-licensing transactions related to the TRACER capsids. To maximize the potential of TRACER capsids for the Company’s own programs and out-licensing transactions, the Company has retained to date, and expects to retain in the future, all rights associated with such TRACER capsids other than the rights specific to their use in combination with a particular licensee’s transgenes.

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 a history of incurring annual net operating losses. As of June 30, 2022, the Company had an accumulated deficit of \$387.5 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 fees, milestone payments, and cost reimbursements associated with its prior collaborations with Sanofi Genzyme Corporation (“Sanofi Genzyme”) and AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company (collectively, “AbbVie”), and its ongoing collaboration with Neurocrine, its licensing agreement with Pfizer, and its licensing agreement with Novartis.

Through June 30, 2022, the Company has raised approximately \$724.0 million of proceeds from sales of convertible preferred stock and common stock, including its initial public offering and follow-on public offering, and from its collaboration and license agreements. As of June 30, 2022, the Company had cash, cash equivalents, and marketable securities of \$148.1 million.

Based upon its current operating plan, the Company expects that its existing cash, cash equivalents, and marketable securities at June 30, 2022, together with amounts expected to be received as reimbursement for development costs under the Neurocrine Collaboration Agreement, will be sufficient to meet the Company’s planned operating expenses and capital expenditure requirements into 2024.

There can be no assurance that the Company will be able to obtain additional debt or equity financing on terms acceptable to the Company or generate product revenue or revenue from collaboration partners, 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. 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 fiscal year ended December 31, 2021 as filed with the Securities and Exchange Commission (“SEC”) on March 8, 2022. These interim condensed consolidated financial statements, in the opinion of management, reflect all normal recurring adjustments necessary for a fair presentation of the Company’s financial position and results of operations for the periods presented. Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Updates (“ASU”) of the Financial Accounting Standards Board (“FASB”).

### *Principles of Consolidation*

The unaudited interim consolidated financial statements include the accounts of the Company and its wholly owned subsidiary as disclosed in Note 2, under the heading “Summary of Significant Accounting Policies - 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, 2021. 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 Note 2, "Summary of Significant Accounting Policies," within the "Notes to Consolidated Financial Statements" accompanying the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

**3. Fair value measurements**

Assets and liabilities measured at fair value on a recurring basis as of June 30, 2022 and December 31, 2021 are as follows:

<b>Assets</b>	<b>Total</b>	<b>Quoted Prices in Active Markets for Identical Assets (Level 1)</b>	<b>Significant Other Observable Inputs (Level 2)</b>	<b>Significant Unobservable Inputs (Level 3)</b>
<i>(in thousands)</i>				
<b>June 30, 2022</b>				
Money market funds included in cash and cash equivalents	\$ 75,562	\$ 75,562	\$ —	\$ —
Marketable securities - U.S. Treasury notes	69,727	69,727	—	—
Total	\$ 145,288	\$ 145,288	\$ —	\$ —
<b>December 31, 2021</b>				
Money market funds included in cash and cash equivalents	\$ 100,305	\$ 100,305	\$ —	\$ —
Marketable securities - U.S. Treasury notes	15,106	15,106	—	—
Total	\$ 115,411	\$ 115,411	\$ —	\$ —

The Company measures the fair value of money market funds and U.S. Treasury notes based on quoted prices in active markets for identical securities.

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

Cash, cash equivalents, and marketable securities included the following at June 30, 2022 and December 31, 2021:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	<i>(in thousands)</i>			
<b>As of June 30, 2022</b>				
Money market funds included in cash and cash equivalents	\$ 75,562	\$ —	\$ —	\$ 75,562
Marketable securities - U.S. Treasury notes	69,962	—	(236)	69,727
Total money market funds and marketable securities	<u>\$ 145,524</u>	<u>\$ —</u>	<u>\$ (236)</u>	<u>\$ 145,288</u>
<b>As of December 31, 2021</b>				
Money market funds included in cash and cash equivalents	\$ 100,305	—	—	\$ 100,305
Marketable securities - U.S. Treasury notes	15,117	—	(11)	15,106
Total money market funds and marketable securities	<u>\$ 115,422</u>	<u>\$ —</u>	<u>\$ (11)</u>	<u>\$ 115,411</u>

All of the Company's marketable securities as of June 30, 2022, have a contractual maturity of one year or less.

The Company reviews investments whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. In connection with these investments, the Company evaluates whether the decline in fair value has resulted from credit losses or other factors, considering the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and adverse conditions specifically related to the security, among other factors. If this assessment indicates that a credit loss exists, the present value of cash flows expected to be collected from the security is compared to the amortized cost basis of the security. If the present value of cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for credit losses is recorded for the credit loss on the condensed consolidated balance sheet, limited by the amount that the fair value is less than the amortized cost basis. Any impairment that is not related to credit is recognized in other comprehensive (loss) income. Changes in the allowance for credit losses are recorded as a provision for (or reversal of) credit loss expense in general and administrative expenses within the condensed consolidated statement of operations. Losses are charged against the allowance when the Company believes the uncollectability of an available-for-sale security is confirmed or when either of the criteria regarding intent or requirement to sell is met.

The Company held \$70.0 million and \$15.1 million marketable securities that were in an unrealized loss position as of June 30, 2022 and December 31, 2021, respectively. The unrealized losses at June 30, 2022 and December 31, 2021 were attributable to changes in interest rates and the unrealized losses do not represent credit losses. The Company does not intend to sell these securities and it is not more likely than not that it will be required to sell them before recovery of their amortized cost basis.

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, 2022	As of December 31, 2021
	<i>(in thousands)</i>	
Cash and cash equivalents	\$ 78,329	\$ 117,433
Restricted cash included in deposits and other non-current assets	1,515	1,779
Total cash, cash equivalents, and restricted cash	<u>\$ 79,844</u>	<u>\$ 119,212</u>

## 5. Accrued expenses

Accrued expenses as of June 30, 2022 and December 31, 2021 consist of the following:

	<u>As of June 30,</u> <u>2022</u>	<u>As of December 31,</u> <u>2021</u>
	<i>(in thousands)</i>	
Employee compensation costs	\$ 2,800	\$ 5,022
Research and development costs	3,662	3,719
Professional services	344	727
Accrued goods and services	379	1,482
Total	<u>\$ 7,185</u>	<u>\$ 10,950</u>

## 6. Lease obligation

### *Operating Leases*

As of June 30, 2022, the Company has a lease for office and lab space at 64 Sidney Street in Cambridge, Massachusetts through November 30, 2026 and a lease for additional laboratory and office space at 75 Hayden Avenue in Lexington, Massachusetts through January 31, 2031.

In September 2021, the Company entered into an agreement with BioNTech US, Inc. (“BioNTech US”) to sublease part of the office and lab space leased by the Company at 75 Sidney Street in Cambridge, Massachusetts (the “Sublease Agreement”) at that time. The sublease term was for approximately 3.3 years. The sublease did not relieve the Company of its original obligation under the lease, and therefore the Company did not adjust the operating lease right-of-use asset as a result of the sublease and accounted for the sublease as a separate lease.

On June 22, 2022 the Company entered into a Lease Termination Agreement (the “Lease Termination Agreement”) and terminated the lease for office and lab space at 75 Sidney Street (the “75 Sidney Street Lease”), effective immediately. The 75 Sidney Street Lease was previously scheduled to terminate, in accordance with its terms, on November 30, 2026. In connection with the Lease Termination Agreement, the Company also entered into a Sublease Termination Agreement (the “Sublease Termination Agreement”) and terminated the Sublease Agreement with BioNTech US. The Company did not incur any termination penalties in connection with the Lease Termination Agreement or Sublease Termination Agreement. The Company derecognized the related right-of-use asset of approximately \$14.5 million and the operating lease liabilities of \$17.0 million, accordingly, resulting in a gain of \$2.5 million in the three-month period ended June 30, 2022.

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 its landlords as security for the performance of its obligations under the leases. Approximately \$0.3 million relates to the letter of credit held for the 75 Sidney Street Lease, which is included in prepaid expenses and other current assets in the accompanying condensed balance sheets. The remaining \$1.5 million is recorded as restricted cash and included in deposits and other non-current assets in the accompanying condensed consolidated balance sheets.

During the three and six months ended June 30, 2022, the Company incurred lease expenses of \$1.4 million and \$2.8 million, respectively, for operating leases. During the three and six months ended June 30, 2021, the Company incurred lease expenses of \$1.9 million and \$3.7 million, respectively, for operating leases. As of June 30, 2022, the weighted average remaining lease term was 6.5 years and the weighted average incremental borrowing rate used to determine the operating lease liability was 7.4%.

The following table summarizes the operating sublease income generated under the Sublease Agreement for the three and six months ended June 30, 2022 and 2021:

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2022	2021	2022	2021
Operating sublease income	<i>(in thousands)</i>			
	\$ 690	\$ —	\$ 1,380	\$ —

## 7. Other liabilities

As of June 30, 2022 and December 31, 2021, other current and non-current liabilities consisted of the following:

	As of June 30,		As of December 31,	
	2022	2021	2021	2021
	<i>(in thousands)</i>			
<b>Other current liabilities</b>				
Lease liability		2,526		5,571
Total other current liabilities	\$	2,526	\$	5,571
<b>Other non-current liabilities</b>				
Lease liability	\$	21,741	\$	38,608
Other		1,000		1,001
Total other non-current liabilities	\$	22,741	\$	39,609

## Strategic Restructuring

On August 6, 2021, the board of directors of the Company approved a strategic restructuring plan to eliminate a portion of its workforce as part of an initiative to reduce expenses and enhance operations. The strategic restructuring plan was approved in connection with its portfolio reevaluation efforts and its strategic shift to invest additional resources in the Company's TRACER capsid development efforts.

During the year ended December 31, 2021, the Company incurred restructuring costs of approximately \$2.6 million, which consists of severance-related costs. Substantially all costs have been paid as of June 30, 2022.

## 8. Commitments and contingencies

### Significant Agreements

#### 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 agreed to collaborate on the conduct of four collaboration programs (the "Neurocrine Programs") which include: (i) VY-AADC (NBIb-1817) for Parkinson's disease (the "VY-AADC Program"), (ii) VY-FXN01 for Friedrich's ataxia (the "FA Program") (collectively, with the VY-AADC Program, the "Legacy 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 collaboration agreement with Sanofi Genzyme (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.

In February 2021, Neurocrine notified the Company that it had elected to terminate the Neurocrine Collaboration Agreement solely with regards to the VY-AADC Program, effective August 2, 2021 (the “Neurocrine VY-AADC Program Termination Effective Date”). The Neurocrine Collaboration Agreement remains in full force and effect for each other program thereunder. As a result of the termination, Neurocrine is no longer obligated to reimburse the Company for research and development activities related to the VY-AADC Program.

Under the terms of the Neurocrine Collaboration Agreement, the Company originally 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. As a result of the termination of the Neurocrine Collaboration Agreement with regards to the VY-AADC Program, in accordance with the terms of the Neurocrine Collaboration Agreement, the licenses granted by the Company to Neurocrine regarding the VY-AADC Program have expired, and the Company has regained worldwide intellectual property rights regarding the VY-AADC Program, in each case as of the VY-AADC Termination Effective Date.

Pursuant to development plans agreed by the parties, which are 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 for each Neurocrine Program, 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. As a result of Neurocrine’s termination of the Neurocrine Collaboration Agreement with respect to the VY-AADC Program, the Transition Event with respect to the VY-AADC Program is no longer applicable. The Transition Events for the remaining programs are (i) with respect to the FA Program, the Company’s receipt of topline data for the initial Phase 1 clinical trial for an FA Program product candidate; and (ii) with respect to each Discovery Program, the preparation by the Company and the approval by Neurocrine of an investigational new drug (“IND”) application to be filed with the U.S. Food and Drug Administration (the “FDA”) by Neurocrine for the first development candidate in such Discovery Program. For the FA Program, the Company was granted the option (the “FA Co-Co Option”) to co-develop and co-commercialize the FA Program upon the occurrence of a specified event (a “FA Co-Co Trigger Event”). The Company agreed, upon its exercise of the FA Co-Co Option, to enter into a cost- and profit-sharing arrangement with Neurocrine (the “FA Co-Co Agreement”), and (i) jointly develop and commercialize the Collaboration Products for the FA Program (“FA Collaboration Products”), (ii) share in its costs, profits and losses, and (iii) forfeit certain milestones and royalties on net sales in the United States during the effective period of the FA Co-Co Agreement. The FA Co-Co Trigger Event is the receipt of topline data for the initial Phase 1 clinical trial for an FA Program product candidate.

Under the Neurocrine Collaboration Agreement, subject to exceptions specified therein, the Company and Neurocrine agreed that profits and losses under the Company’s FA Co-Co Option would be allocated 60% to Neurocrine and 40% to the Company for any FA Collaboration Product. The parties agreed that FA Co-Co Agreement would 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 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.

Under the Neurocrine Collaboration Agreement, the parties committed to agree on a list of up to eight target genes (the "Targets") from which Neurocrine had the right to nominate Targets for the two Discovery Programs. The Company and Neurocrine completed the nomination process, and the JSC has approved two Targets for development under the Discovery Programs. The two Targets are currently under development.

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, which the Company is no longer eligible to receive in light of the partial termination of the Neurocrine Collaboration Agreement; (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 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 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 (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. As a result of Neurocrine's termination of the Neurocrine Collaboration Agreement with respect to the VY-AADC Program, the Company is no longer entitled to receive royalties related to the VY-AADC Program. 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 any FA Co-Co Agreement. 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) with respect to the FA Program, if an FA Co-Co Agreement is in effect, Neurocrine can terminate the FA Co-Co Agreement for such program and the Company would no longer have co-development and co-commercialization rights with respect to the FA Collaboration Products and (ii) subject to any license agreements, Neurocrine would no longer have any obligations with respect to any Collaboration Products resulting from such program.

#### *Termination of VY-AADC Program*

As described above, as of the Neurocrine VY-AADC Program Termination Effective Date, the license granted by the Company to Neurocrine thereunder regarding the VY-AADC Program expired, the Company regained worldwide intellectual property rights regarding the VY-AADC Program, and the restrictions on the Company to develop, manufacture or commercialize a gene therapy product directed to the target of the VY-AADC Program terminated, in each case in accordance with the terms of the Neurocrine Collaboration Agreement. As of the Neurocrine VY-AADC Program Termination Effective Date, Neurocrine no longer is obligated to reimburse the Company for research and development activities related to the VY-AADC Program, and the Company is no longer entitled to receive future milestone or royalty payments related to the VY-AADC Program. The Company is supporting Neurocrine, the study sponsor and IND holder, on ongoing matters related to the completion of imaging and clinical assessments requested by the Data Safety and Monitoring Board (the "DSMB"), and the provision of other information requested by the FDA for the RESTORE-1 Phase 2 clinical trial.

#### *Accounting Analysis*

At inception, the Neurocrine Collaboration Agreement included the following performance obligations: (i) research and development services for each Legacy 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 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 cost incurred under the agreed upon program plans. The Company utilized the most likely amount approach and estimated the expected cost reimbursement to be \$431.1 million at inception. The Company 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 fourth quarter of 2021, the Company further revised the estimate of the expected reimbursement to approximately \$80 million based on expectations resulting from decisions made at the JSC meeting in the fourth quarter of 2021, which are expected to result in significantly less research and development services being provided by the Company under the Neurocrine Collaboration Agreement. As of June 30, 2022, the estimate of the expected reimbursement is \$79.7 million based on expectations as of such date. 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 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, which 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 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 Agreement. 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 as of June 30, 2022:

<u>Performance Obligation</u>	<u>Amount</u>
	<i>(in thousands)</i>
Variable Consideration	
VY-AADC Program	\$ 53,863
FA Program	17,088
Discovery Program 1	5,355
Discovery Program 2	3,362
Total	<u>\$ 79,668</u>

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:

<u>Performance Obligation</u>	<u>Amount</u>
	<i>(in thousands)</i>
Fixed Consideration	
VY-AADC Program	\$ 49,045
FA Program	20,647
Discovery Program 1	14,443
Discovery Program 2	8,247
Total	<u>\$ 92,382</u>

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.

The Company determined the partial termination of the Neurocrine Collaboration Agreement with respect to the VY-AADC Program represented a modification of the arrangement under ASC 606 and that the remaining fixed transaction price at the Neurocrine VY-AADC Program Termination Effective Date of \$42.2 million should be re-allocated to the FA Program and Discovery Program 1 and 2 based on their standalone selling prices. Accordingly, the Company recorded a cumulative adjustment to revenue of approximately \$0.9 million on the partially satisfied remaining performance obligations, as the remaining services to be performed under each of the performance obligations are not distinct from the services prior to the modification. The Company determined that reasonable changes to the Company's estimates of standalone selling prices for the FA Program, Discovery Program 1 and Discovery Program 2 performance obligations did not have a material impact on the re-allocation or the amount of revenue recorded pursuant to the cumulative catch-up adjustment.

During the three and six months ended June 30, 2022, the Company recognized \$0.7 million and \$1.4 million, respectively, of revenue 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, 2021, the Company recognized \$1.4 million and \$7.9 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.

The following table presents changes in the balances of the Company's related party collaboration receivables and contract liabilities during the six months ended June 30, 2022:

	Balance at December 31, 2021	Additions	Deductions	Balance at June 30, 2022
		<i>(in thousands)</i>		
Related party collaboration receivable	\$ 732	\$ 358	(939)	\$ 151
Contract liabilities:				
Deferred revenue	\$ 12,096	-	(1,214)	\$ 10,881

The change in the receivable balance for the six months ended June 30, 2022 is primarily driven by amounts owed to the Company for research and development services provided, offset by amounts collected from Neurocrine during the period.

Costs incurred relating to the Company's collaboration programs under the Neurocrine Collaboration Agreement 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 statements of operations during the three and six months ended June 30, 2022.

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.

## **Pfizer Option and License Agreement**

### *Summary of Agreement*

On October 1, 2021, the Company entered into an option and license agreement with Pfizer (the "Pfizer License Agreement"), pursuant to which the Company has granted Pfizer options to receive an exclusive license (the "Pfizer License Options") to certain TRACER capsids to develop and commercialize certain AAV gene therapy candidates comprised of a capsid and specified Pfizer transgenes (the "Pfizer Transgenes"). Under the terms of the Pfizer License Agreement, Pfizer intends to evaluate the potential use of the capsids in combination with up to two Pfizer Transgenes to help treat respective central nervous system and cardiovascular diseases.

Under the Pfizer License Agreement, the Company has agreed to provide Pfizer with certain quantities of materials encoding specified existing capsids for Pfizer's evaluation. During the research term, which extends until October 1, 2022, or, in the event Pfizer exercises a Pfizer License Option, until October 1, 2024, the Company may, at its sole discretion and expense, conduct additional research activities to identify additional proprietary capsids that may be useful for AAV gene therapies for the treatment of central nervous system or cardiovascular diseases. The Company has agreed to disclose to Pfizer, on a rolling basis, the performance characteristics identified during the research term for all such capsid candidates. Following such disclosure, Pfizer has the right, in its sole discretion, to select any capsid candidate for evaluation to determine its interest in exercising a Pfizer License Option with respect to such capsid candidate. Pfizer may exercise up to two Pfizer License Options, provided that it may exercise only one Pfizer License Option for each Pfizer Transgene. The Company has granted Pfizer, effective upon Pfizer's exercise of a Pfizer License Option, with respect to a capsid candidate for the Pfizer Transgene identified therein, an exclusive, worldwide license, with the right to sublicense, under certain of the Company's intellectual property, the rights to develop and commercialize the applicable licensed capsid as incorporated into products containing the corresponding Pfizer Transgene (the "Pfizer Licensed Products"). Additionally, upon such Pfizer License Option exercise, the Company and Pfizer have agreed that the Company shall provide certain additional know-how that has not been previously provided to

Pfizer to enable Pfizer to exploit such licensed capsid and the corresponding Pfizer Transgene for use in a Pfizer Licensed Product. Upon the exercise of a Pfizer License Option, until October 1, 2024, while the Company is not obligated to conduct additional research activities upon option exercise to identify additional proprietary capsids that may be useful for AAV gene therapies for the treatment of central nervous system or cardiovascular diseases, it has agreed to continue to disclose to Pfizer, on a rolling basis, the performance characteristics identified for all such capsid candidates, if and when available. Pfizer may, during the research term conduct additional evaluation of such capsid candidates and has the right to substitute any other capsid candidate for the capsid it previously elected to license when it exercised the Pfizer License Option.

Under the Pfizer License Agreement, Pfizer is solely responsible for, and has sole decision-making authority with respect to, development and commercialization of the Pfizer Licensed Products. In the event Pfizer exercises a Pfizer License Option, Pfizer is required to use commercially reasonable efforts to develop and obtain regulatory approval for at least one Pfizer Licensed Product for each Pfizer Transgene for which Pfizer has exercised its Pfizer License Option in (i) the United States and (ii) at least one of the following countries: the United Kingdom, France, Germany, Italy, Spain and Japan (each of which, a “Pfizer Major Market Country”), subject to certain limitations. Pfizer is also required to use commercially reasonable efforts to commercialize each Pfizer Licensed Product in the United States and at least one Pfizer Major Market Country where Pfizer or its designated affiliates or sublicensees has received regulatory approval for such Pfizer Licensed Product, subject to certain limitations.

Under the terms of the Pfizer License Agreement, Pfizer paid the Company an upfront payment of \$30.0 million in October 2021. Pfizer has also agreed to pay the Company, upon each Pfizer License Option exercise, a fee of \$10.0 million. Following each Pfizer License Option exercise, with respect to a Pfizer Transgene, the Company is also eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of \$115.0 million for the first corresponding Pfizer Licensed Product to achieve the corresponding milestone. On a Pfizer Licensed Product-by-Pfizer Licensed Product basis, the Company is also eligible to receive (a) specified sales milestone payments of up to an aggregate of \$175.0 million per Pfizer Licensed Product and (b) tiered, escalating royalties in the mid- to high-single-digit percentages of annual net sales of each Pfizer Licensed Product. The royalties are subject to potential reductions in customary circumstances including patent claim expiration, payments for certain third-party licenses, and biosimilar market penetration, subject to specified limits.

Under the terms of the Pfizer License Agreement, each the Company and Pfizer owns the entire right, title, and interest in and to all patents or know-how controlled by such party and existing as of or before the effective date of the Pfizer License Agreement, or invented, developed, created, generated or acquired solely by or on behalf of such party after such effective date.

Subject to certain specified exceptions, any patents and know-how that are invented or otherwise developed jointly by or on behalf of the parties during the term of the Pfizer License Agreement and in the course of the Company’s and Pfizer’s activities under the Pfizer License Agreement will follow inventorship under U.S. patent law. Subject to certain limitations and exceptions, the Company agreed (i) during the research term, not to conduct any internal program or program on behalf of a third party that is directed to development or commercialization of any capsid candidates, or grant any third party or affiliate any right or license under the Company’s rights in such capsid candidates to exploit any therapeutic product, in combination with any Pfizer Transgene in any indication for therapeutic, diagnostic and prophylactic human and veterinary use; and (ii) after Pfizer’s exercise of a Pfizer License Option, not to grant any third party or affiliate any right or license under the Company’s patents to exploit any licensed capsid in combination with any Pfizer Transgene.

Unless earlier terminated, the Pfizer License Agreement expires on the earlier to occur of (i) the first anniversary of the effective date of the Pfizer License Agreement, if no Pfizer License Option is exercised, and (ii) the expiration of the last-to-expire royalty term with respect to all Pfizer Licensed Products in all countries if at least one Pfizer License Option is exercised. Subject to a cure period, either party may terminate the Pfizer License Agreement, in whole or in part, subject to specified conditions, in the event of the other party’s uncured material breach. Pfizer may also terminate the Pfizer License Agreement, in whole or in part, subject to specified conditions, for the Company’s insolvency, the occurrence of a violation of global trade control laws, or for the Company’s noncompliance with certain anti-bribery or anti-corruption covenants. Pfizer may also terminate the Pfizer License Agreement, in whole or in part, for any or no reason upon ninety days’ written notice to us.

Upon certain terminations for cause by Pfizer, the licenses that the Company has granted to Pfizer under the Pfizer License Agreement shall become irrevocable and perpetual, and all milestone payments and royalties that would have otherwise been payable by Pfizer under such licenses had the Pfizer License Agreement remained in effect would be substantially reduced.

*Accounting Analysis*

The Company assessed the promised goods and services under the Pfizer License Agreement, in accordance with ASC 606, and determined that the Pfizer License Agreement contains two performance obligations consisting of two material rights, one for each of the Pfizer License Options. The Company concluded that each Pfizer License Option provides a material right as consideration for each option is less than the amount that the Company would otherwise have expected to receive outside the context of the contract. The promises at inception do not include the underlying goods or services that would be delivered upon exercise of the option, but rather represent the value to the customer of having the right to exercise the Pfizer License Option at the specified exercise fee. Upon the exercise of a Pfizer License Option, until October 1, 2024, while the Company is not obligated to conduct additional research activities upon option exercise to identify additional proprietary capsids that may be useful for AAV gene therapies for the treatment of central nervous system or cardiovascular diseases, it has agreed to continue to disclose to Pfizer, on a rolling basis, the performance characteristics identified for all such capsid candidates, if and when available. Pfizer may, conduct additional evaluation of such capsid candidates and has the right to substitute any other capsid candidate for the capsid it previously elected to license when it exercised the Pfizer License Option. The Company determined that this promise to provide Pfizer the ability to evaluate and potentially substitute other capsid candidates for the capsid it previously elected to license when it exercised the Pfizer License Option, if and when available, is an additional performance obligation in the arrangement (“the Pfizer Substitution Right Performance Obligation”).

The Company received a nonrefundable, upfront payment of \$30.0 million as consideration under the Pfizer License Agreement, which represents the transaction price at inception. Additional consideration to be paid to the Company upon exercise of the Pfizer License Options or upon reaching certain milestones are excluded from the transaction price as they relate to option fees and milestones that could only be achieved subsequent to an option exercise.

The Company allocated the transaction price to the two material rights based on their relative standalone selling prices. The estimated standalone selling price for each material right was based on an adjusted market assessment approach. The Company concluded that the market would be willing to pay an equal amount for each Pfizer License Option on a standalone basis. The Company reached this conclusion after considering (i) the downstream economics including option fees, milestones and royalties related to each Pfizer License Option being identical and (ii) comparable market data. The Company determined the standalone selling price for the Pfizer Substitution Right Performance Obligation was insignificant to the allocation of the transaction price using the relative standalone selling price model and, accordingly, did not allocate any transaction price to the Pfizer Substitution Right Performance Obligation. This determination was supported by qualitative and quantitative assessments of the standalone selling price that considered the cost of identifying other potential capsid candidates and the likelihood of license substitution. As such, based on the relative standalone selling price for each of the two material rights, the allocation of the transaction price to the separate performance obligations is \$15.0 million for each material right.

The amount allocated to each material right was recorded as deferred revenue and will be recognized either upon exercise of the Pfizer License Option or upon expiration of the Pfizer License Option.

During the three and six months ended June 30, 2022, the Company did not recognize any revenue related to the Pfizer License Agreement. As of June 30, 2022, the entire transaction price of \$30.0 million is recorded as deferred revenue, current in the accompanying consolidated balance sheet.

## **Novartis Option and License Agreement**

### *Summary of Agreement*

On March 4, 2022 (the “Novartis Effective Date”), the Company entered into an option and license agreement with Novartis (the “Novartis License Agreement”). Pursuant to the Novartis License Agreement, the Company has granted Novartis options (the “Novartis License Options”) to license TRACER capsids (“Novartis Licensed Capsids”) for exclusive use with certain targets to develop and commercialize adeno-associated virus gene therapy candidates comprised of Novartis Licensed Capsids and payloads directed to such targets (the “Novartis Payloads”).

During the period commencing on the Novartis Effective Date and ending on the first anniversary thereof or, in the event Novartis exercises a Novartis License Option, the third anniversary thereof (the “Novartis Research Term”), the Company has granted Novartis a non-exclusive research license to evaluate the Company’s TRACER capsids for potential use, in combination with Novartis Payloads, in programs targeting three specified genes (the “Initial Novartis Targets”). Upon the payment of additional fees, Novartis may also assess the Company’s TRACER capsids for use with two other targets (the “Additional Novartis Targets”), subject to certain conditions including that such target is not part of, or reasonably competitive with, the Company’s current development programs (the Initial Novartis Targets and the Additional Novartis Targets collectively, the “Novartis Targets”). During the Novartis Research Term, the Company may, at its sole discretion and expense, conduct further research activities to identify additional TRACER capsids. If the Company elects to do so, the Company has agreed to disclose performance characteristics of such new TRACER capsids to Novartis on a rolling basis.

During the Novartis Research Term, Novartis may exercise up to three Novartis License Options—or up to five Novartis License Options if Novartis is evaluating the Additional Novartis Targets—in the aggregate, provided that Novartis may only exercise one Novartis License Option for each Novartis Target. Upon the exercise of any Novartis License Option, the Company has agreed to grant Novartis a target-exclusive, worldwide license, with the right to sublicense, under certain of the Company’s intellectual property, the rights to develop and commercialize the applicable Novartis Licensed Capsid as incorporated into products containing the corresponding Novartis Payload (the “Novartis Licensed Products”). Upon the exercise of a Novartis License Option, the Company has agreed to provide certain additional know-how to enable Novartis to exploit the Novartis Licensed Capsid and the corresponding Novartis Payload for use in a Novartis Licensed Product. Novartis may, during the Novartis Research Term but following the exercise of a Novartis License Option, conduct additional evaluation of the Company’s capsid candidates and has the right to substitute any other TRACER capsid for a Novartis Licensed Capsid.

Subject to the Company’s disclosure obligations described above, the Company and Novartis have agreed to conduct their respective research and evaluation activities independently, with communications being managed by two alliance managers comprised of a designee from each of the Company and Novartis.

Under the Novartis License Agreement, Novartis is solely responsible for, and has sole decision-making authority with respect to, development and commercialization of the Novartis Licensed Products. In the event Novartis exercises a Novartis License Option, Novartis is required to use commercially reasonable efforts to develop and obtain regulatory approval for at least one Novartis Licensed Product for each Novartis Target for which it has exercised a Novartis License Option in (i) the United States and (ii) at least three of the following countries: the United Kingdom, France, Germany, Italy, Spain and Japan (each of which, a “Novartis Major Market Country”), subject to certain limitations. Novartis is also required to use commercially reasonable efforts to commercialize each Novartis Licensed Product in the United States and at least three Novartis Major Market Countries where Novartis or its designated affiliates or sublicensees has received regulatory approval for such Novartis Licensed Product, subject to certain limitations.

During the Novartis Research Term, the Company has agreed to provide plasmids to Novartis for the production of TRACER capsids for evaluation upon request. The Company has also granted Novartis a non-exclusive license, effective upon an exercise of a Novartis License Option and in addition to its options for target-exclusive licenses under certain of the Company’s intellectual property described above, on a Novartis Licensed Capsid-by-Novartis Licensed Capsid basis, under certain of the Company’s know-how to exploit the applicable Novartis Licensed Capsid as incorporated into Novartis Licensed Products containing the corresponding Novartis Payload.

Under the terms of the Novartis License Agreement, Novartis paid the Company an upfront payment of \$54 million. Novartis has also agreed to pay the Company a fee of \$18.0 million per Additional Novartis Target it elects to add to the collaboration and, upon each exercise of a Novartis License Option, an option exercise fee of \$12.5 million. Following each exercise of a Novartis License Option, the Company is also eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of \$125.0 million for the first corresponding Novartis Licensed Product to achieve the corresponding milestone. On a Novartis Licensed Product-by-Novartis Licensed Product basis, the Company is also eligible to receive (a) specified sales milestone payments of up to an aggregate of \$175.0 million per Novartis Licensed Product and (b) tiered, escalating royalties in the mid- to high-single-digit percentages of annual net sales of each Novartis Licensed Product. The royalties are subject to potential reductions in customary circumstances including patent claim expiration, payments for certain third-party licenses, and biosimilar market penetration, subject to specified limits.

Under the terms of the Novartis License Agreement, each party owns the entire right, title, and interest in and to all patents or know-how controlled by such party and existing as of or before the Novartis Effective Date, or invented, developed, created, generated or acquired solely by or on behalf of such party after the Novartis Effective Date. Subject to certain specified exceptions, any patents and know-how that are invented or otherwise developed jointly by or on behalf of the parties during the term of the Novartis License Agreement and in the course of the parties' activities under the Novartis License Agreement will follow inventorship under U.S. patent law.

Subject to certain limitations and exceptions, the Company has agreed (i) during the Novartis Research Term, not to conduct any internal program or program on behalf of a third party that is directed to the development or commercialization of any Company's capsids, or grant any third party or affiliate any right or license under the Company's rights in such capsids, to exploit any therapeutic product containing a capsid in combination with a payload designed to have therapeutic effect on any of the Novartis Targets; and (ii) after Novartis's exercise of any Novartis License Option, not to grant any third party or affiliate any right or license under the Company's patents to exploit any Novartis Licensed Capsid for the applicable Novartis Target.

Unless earlier terminated, the Novartis License Agreement expires on the earlier to occur of (i) the first anniversary of the Novartis Effective Date, if no Novartis License Option is exercised, and (ii) the expiration of the last-to-expire royalty term with respect to all Novartis Licensed Products in all countries if at least one Novartis License Option is exercised. Subject to a cure period, either party may terminate the Novartis License Agreement, in whole or in part, subject to specified conditions, in the event of the other party's uncured material breach. Novartis may also terminate the Novartis License Agreement, in whole or in part, subject to specified conditions, for the Company's insolvency, the occurrence of a violation of global trade control laws, or for the Company's non-compliance with certain anti-bribery or anti-corruption covenants. Novartis may terminate the Novartis License Agreement, in whole or in part, for any or no reason upon ninety days' written notice to the Company.

Upon certain terminations for cause by Novartis, the licenses granted by the Company to Novartis under the Novartis License Agreement shall become irrevocable and perpetual, and all milestone payments and royalties that would have otherwise been payable by Novartis under such licenses had the Novartis License Agreement remained in effect would be substantially reduced.

#### *Accounting Analysis*

The Company assessed the promised goods and services under the Novartis License Agreement, in accordance with ASC 606, and determined that the Novartis License Agreement contains three performance obligations consisting of three material rights, one for each of the Novartis License Options. The Company concluded that each Novartis License Option provides a material right as consideration for each option is less than the amount that the Company would otherwise have expected to receive outside the context of the contract. The promises at inception do not include the underlying goods or services that would be delivered upon exercise of the option, but rather represent the value to the customer of having the right to exercise the Novartis License Option at the specified exercise fee. Upon the exercise of a Novartis License Option, until March 4, 2025, while the Company is not obligated to conduct additional research activities upon any option exercise to identify additional proprietary capsids that may be useful for AAV gene therapies for the treatment of central nervous system or cardiovascular diseases, it has agreed to continue to disclose to Novartis, on a rolling basis, the performance characteristics identified for all such capsid candidates, if and when available.



Novartis may conduct additional evaluation of such capsid candidates and has the right to substitute any other capsid candidate for the Novartis Licensed Capsid it previously elected to license when it exercised the Novartis License Option. The Company determined that this promise to provide Novartis the ability to evaluate and potentially substitute other capsid candidates for the Novartis Licensed Capsid it previously elected to license when it exercised the Novartis License Option, if and when available, is an additional performance obligation in the arrangement (the “Novartis Substitution Right Performance Obligation”). The Company concluded the options for Additional Novartis Targets are not material rights as the price reflects the standalone selling price of the options. The Company will therefore account for the options for Additional Novartis Targets separately, if exercised.

The Company received a nonrefundable, upfront payment of \$54.0 million as consideration under the Novartis License Agreement, which represents the transaction price at inception. Additional consideration to be paid to the Company upon exercise of the Novartis License Options or upon reaching certain milestones are excluded from the transaction price as they relate to option fees and milestones that could only be achieved subsequent to an option exercise.

The Company allocated the transaction price to the three material rights based on their relative standalone selling prices. The estimated standalone selling price for each material right was based on an adjusted market assessment approach. The Company concluded that the market would be willing to pay an equal amount for each Novartis License Option on a standalone basis. The Company reached this conclusion after considering (i) the downstream economics including option fees, milestones and royalties related to each Novartis License Option being identical and (ii) comparable market data. The Company determined the standalone selling price for the Novartis Substitution Right Performance Obligation was insignificant to the allocation of the transaction price using the relative standalone selling price model and did not allocate any transaction price to the Novartis Substitution Right Performance Obligation, accordingly. This determination was supported by qualitative and quantitative assessments of the standalone selling price that considered the cost of identifying other potential capsid candidates and the likelihood of license substitution. As such, based on the relative standalone selling price for each of the three material rights, the allocation of the transaction price to the separate performance obligations is \$18.0 million for each material right.

The amount allocated to each material right was recorded as deferred revenue and will be recognized either upon exercise of the Novartis License Option or upon expiration of the Novartis License Option.

During the three and six months ended June 30, 2022, the Company did not recognize any revenue related to the Novartis License Agreement. As of June 30, 2022, the entire transaction price of \$54.0 million is recorded as deferred revenue, current in the accompanying consolidated balance sheet.

### **Other Agreements**

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 was not a party to any material legal matters or claims as of June 30, 2022 or December 31, 2021. The Company did not have contingency reserves established for any litigation liabilities as of June 30, 2022 or December 31, 2021.

## 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,	
	2022	2021	2022	2021
	<i>(in thousands)</i>			
Research and development	\$ 781	\$ 1,336	\$ 1,582	\$ 2,706
General and administrative	1,709	2,655	3,227	4,886
Total stock-based compensation expense	<u>\$ 2,490</u>	<u>\$ 3,991</u>	<u>\$ 4,809</u>	<u>\$ 7,592</u>

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,	
	2022	2021	2022	2021
	<i>(in thousands)</i>			
Stock options	\$ 1,618	\$ 2,480	\$ 3,095	\$ 5,002
Restricted stock awards and units	842	1,392	1,634	2,366
Employee stock purchase plan awards	30	120	81	223
Total stock-based compensation expense	<u>\$ 2,490</u>	<u>\$ 3,991</u>	<u>\$ 4,809</u>	<u>\$ 7,592</u>

### 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, 2022 was as follows:

	Units	Weighted Average Grant Date Fair Value Per Unit
Unvested restricted stock units as of December 31, 2021	806,379	\$ 7.26
Granted	739,080	\$ 3.79
Vested	(344,255)	7.45
Forfeited	(169,839)	\$ 5.06
Unvested restricted stock units as of June 30, 2022	<u>1,031,365</u>	\$ 5.08

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. Restricted stock units granted by the Company typically vest in equal amounts, annually over three years. All of the restricted stock units granted in the six months ended June 30, 2022 vest in equal amounts, annually over three or four years. The stock-based compensation expense related to restricted stock units and awards was \$0.8 million and \$1.6 million for the three and six months ended June 30, 2022, respectively. The stock-based compensation expense related to restricted stock units and awards was \$1.4 million and \$2.4 million for the three and six months ended June 30, 2021, respectively.

As of June 30, 2022, the Company had unrecognized stock-based compensation expense related to its unvested restricted stock units of \$4.0 million, which is expected to be recognized over the remaining average vesting period of 2.0 years.

**Stock Options**

The following is a summary of stock option activity for the six months ended June 30, 2022:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	5,013,193	\$ 12.69	5.6	\$ 1,165
Granted	2,965,075	\$ 4.95		
Exercised	(74,496)	\$ 7.90		
Cancelled or forfeited	(1,274,172)	\$ 12.42		
Outstanding at June 30, 2022	<u>6,629,600</u>	\$ 9.33	7.2	\$ 5,914
Exercisable at June 30, 2022	<u>3,378,945</u>	\$ 12.29	5.3	\$ 1,575

As of June 30, 2022, the Company had unrecognized stock-based compensation expense related to its unvested stock options of \$13.0 million which is expected to be recognized over the remaining weighted-average vesting period of 3.1 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,	
	2022	2021
Unvested restricted common stock awards	137,255	156,863
Unvested restricted common stock units	1,031,365	1,170,702
Outstanding stock options	6,629,600	5,919,375
Total	<u>7,798,220</u>	<u>7,246,940</u>

Basic net loss per share for the three and six months ended June 30, 2022 and 2021 is the same as diluted net loss per share as shown on the Company's condensed consolidated statement of operations.

**11. Related-party transactions**

During the three and six months ended June 30, 2022, the Company received scientific advisory board and other scientific advisory services from one of its prior executives, Dinah Sah, Ph.D., the Company's former Chief Scientific Officer. The total amount of fees paid to Dr. Sah for services provided during the three and six months ended June 30, 2022, was \$82,425 and \$92,325, respectively. The total amount of fees paid to Dr. Sah for services provided during the three and six months ended June 30, 2021 was \$60,000 and \$90,000, respectively.

During the six months ended June 30, 2022, the Company received advisory services related to strategic planning, operations, and management from Alfred Sandrock, M.D., Ph.D., the Company's current President and Chief Executive Officer and a member of the Company's Board of Directors, before he commenced service in the capacity of President and Chief Executive Officer in March 2022. The total amount of fees paid to Dr. Sandrock for services provided was \$60,000 for the six months ended June 30, 2022.

Under the Neurocrine Collaboration Agreement, the Company and Neurocrine have agreed to conduct research, development and commercialization activities for 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, 2022, the Company had approximately \$0.2 million in related party collaboration receivables associated with Neurocrine.

## 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, 2021, which was filed with the Securities and Exchange Commission, or the SEC, on March 8, 2022.*

*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 gene therapy and neuroscience company developing life-changing treatments and next-generation adeno-associated virus, or AAV, capsids. We focus on diseases where we believe a single dose AAV gene therapy or an antibody can either halt or slow disease progression or reduce symptom severity, therefore providing clinically meaningful impact to patients. Our gene therapy platforms enable us to engineer, optimize, manufacture and deliver AAV-based gene therapies that we believe have the potential to safely provide durable efficacy. Our team of experts in the field of AAV gene therapy and neuroscience first identifies and selects diseases in which we believe an AAV gene therapy or an antibody will answer a high unmet medical need, be supported by target validation, offer an efficient path to human proof of biology, present robust preclinical pharmacology, and offer strong commercial potential. We then engineer and optimize either an AAV vector for delivery of the virus payload to the targeted tissue or cells or a passive antibody for systemic delivery.

We are identifying proprietary AAV capsids, the outer viral protein shells that enclose genetic material of a virus payload. Our team has developed a proprietary AAV capsid discovery platform called TRACER™ (Tropism Redirection of AAV by Cell Type-Specific Expression of RNA) to facilitate the selection of AAV capsids with blood brain barrier, or BBB, crossing and cell-specific transduction properties for particular therapeutic applications. The TRACER discovery platform is a broadly applicable, functional RNA-based AAV capsid discovery platform that allows for rapid *in vivo* evolution of AAV capsids with cell-specific transduction properties in multiple species, including non-human primates. We believe our single dose gene therapies have the potential to be delivered with targeted or systemic surgical delivery or infusions, in conjunction with capsids we discover through our TRACER discovery platform, which we refer to as TRACER capsids.

We are also applying the TRACER discovery platform to identify capsid variant libraries and facilitate the selection of capsids with tropism and transduction in additional cell and tissue types. We are actively engaged in discussions with multiple parties to make TRACER capsids available to third parties for use in their drug development programs through potential licensing and other arrangements.

In addition to our TRACER discovery platform, we have developed a vectorized antibody platform which we believe will overcome many of the challenges of passive immunization. However, we have also seen promising preclinical results from the passive immunization approach and we are investigating both passive immunization and vectorized approaches to administer proprietary antibodies that selectively target pathological tau to address tauopathies.

Our business strategy focuses on discovering, developing, manufacturing and commercializing our gene therapy and antibody programs. As part of this strategy, we have developed core competencies specific to AAV gene therapy development and manufacturing. 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 ongoing collaboration with Neurocrine Biosciences, Inc., which we refer to as Neurocrine, or out-licensing activities including license agreements related to our TRACER capsids with Pfizer Inc., which we refer to as Pfizer, and with Novartis Pharma, AG, which we refer to as Novartis. We believe there is an ongoing opportunity for out-licensing transactions related to the TRACER capsids. To maximize the potential of TRACER capsids for both our own programs and out-licensing transactions, we have retained to date, and expect to retain in the future, all rights associated with such TRACER capsids other than the rights specific to their use in combination with a particular licensee's transgenes. 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 and other diseases to pursue, advancing our product candidates including delivery and manufacturing, and conducting preclinical studies and early-phase clinical trials. We do not have any product candidates approved for sale and have not generated any revenue from product sales, and all of our current product candidates are in the discovery and preclinical development stages.

We have funded our operations primarily through private placements of redeemable convertible preferred stock, public offerings of our common stock, and fees, milestone payments, and cost reimbursements associated with our strategic collaborations, including our prior collaboration with Sanofi Genzyme Corporation, or the Sanofi Genzyme Collaboration, which commenced in February 2015 and was terminated in June 2019, our prior collaboration with AbbVie Biotechnology Ltd. focusing on tau-related disease, or the AbbVie Tau Collaboration, which commenced in February 2018 and was terminated in August 2020, our prior collaboration with AbbVie Ireland Unlimited Company focusing on pathological species of alpha-synuclein, or the AbbVie Alpha-Synuclein Collaboration, which commenced in February 2019 and was terminated in August 2020, our ongoing collaboration with Neurocrine, which commenced in March 2019, our licensing agreement with Pfizer, which commenced in October 2021, and our licensing agreement with Novartis, which commenced in March 2022. We refer to our collaboration agreement with Neurocrine as the Neurocrine Collaboration Agreement. We refer to our licensing agreement with Pfizer as the Pfizer License Agreement, and to our licensing agreement with Novartis as the Novartis License Agreement.

In August 2021, we initiated a strategic reevaluation of our existing product candidate portfolio. As a result of this reevaluation, we have invested additional resources in our TRACER discovery platform to expand our efforts to discover TRACER capsids with broad tissue tropism in central nervous system, or CNS and other tissues. We also announced our plan to advance innovative gene therapy programs that leverage these TRACER capsids as well as our vectorized antibody technology.

We determined in 2021 that we would not advance our VY-AADC program, a gene therapy program for the treatment of Parkinson's disease which we had previously licensed to Neurocrine, on our own. Additionally, to take advantage of our TRACER capsid development efforts, we decided in 2021 to discontinue our VY-HTT01 program for the treatment of Huntington's disease and to initiate a second-generation program for the treatment of Huntington's disease leveraging a proprietary AAV capsid that may enable intravenous administration and achieve broad distribution to affected tissue. We also initiated gene therapy programs using our TRACER capsids in treatment programs for monogenic amyotrophic lateral sclerosis, or ALS, with superoxide dismutase 1, or SOD1, mutations; spinal muscular atrophy, or SMA; and various diseases linked to glucocerebrosidase 1, or GBA1, mutations, including Parkinson's

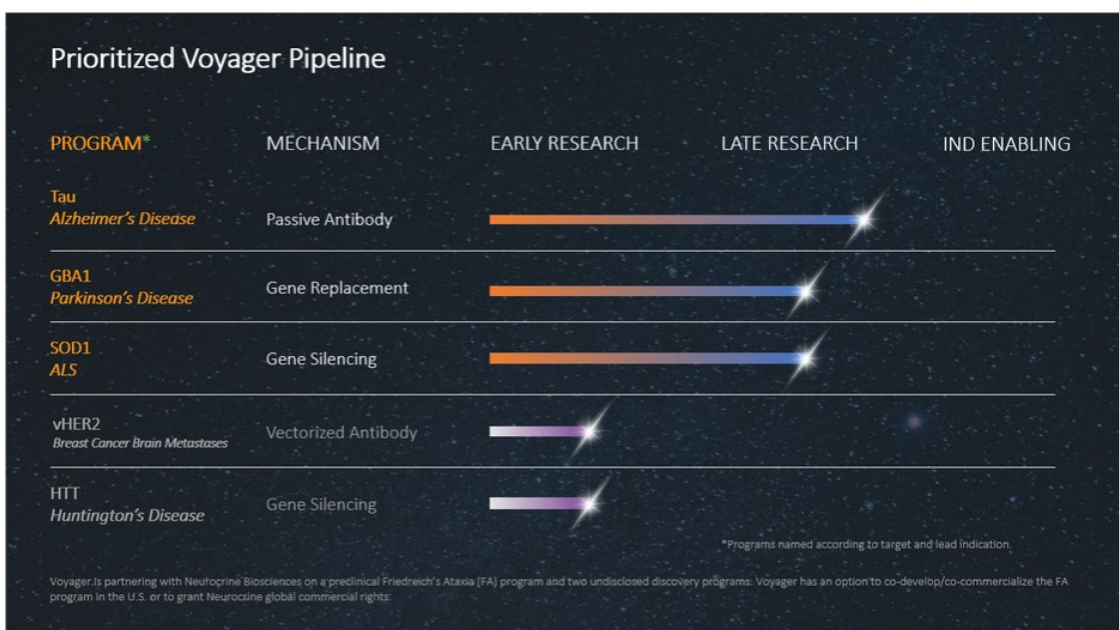
disease. We also determined that we would continue to advance our vectorized antibody platform capability with programs for tauopathies and indications in neuro-oncology.

In August 2022, we announced an updated portfolio strategy prioritizing programs targeting Alzheimer’s disease, Parkinson’s disease with GBA1 mutations, and ALS with SOD1 mutations. This updated portfolio strategy was the result of an in-depth portfolio review. The prioritized programs were selected because each presents a compelling opportunity based on certain criteria identified by the Company, including high unmet medical need, target validation, an efficient path to human proof of biology, robust preclinical pharmacology, and strong commercial potential.

We remain interested in advancing our other programs and are pursuing additional product candidates in the discovery and preclinical stages of development, including our second-generation program for the treatment of Huntington’s disease, our program for the treatment of SMA, and our program for the treatment of human epidermal growth factor receptor positive, or HER2+, brain metastases. We are evaluating opportunities to do so via collaborative partnership, and will continue to conduct preclinical research for our second-generation program for the treatment of Huntington’s disease and our program for the treatment of HER2+ brain metastases. We expect to continue to conduct early preclinical research for our second-generation program for the treatment of SMA as we seek a collaborative partner for the program.

We continue to partner with Neurocrine on programs for diseases including Friedreich’s ataxia. All of our current product candidates are in the early stages of development. We also continue to evaluate additional diseases that could be treated using AAV gene therapy or our proprietary antibodies and are also actively exploring additional potential treatment methods that can utilize our proprietary TRACER capsids.

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



*Overview of Our Pipeline*

We have leveraged our gene therapy platform, our vectorized antibody platform, and our expertise with proprietary antibodies to assemble a pipeline of proprietary AAV gene therapies and passive and vectorized antibodies for the treatment of neurological and other diseases with high unmet medical need. Depending on the disease, our current

AAV gene therapies will use a gene replacement or gene silencing approach, and our current antibodies will use a passive administration or vectorized delivery approach. Our goal is to address the underlying cause or the predominant manifestations of a specific disease by significantly increasing or decreasing expression of the relevant proteins in targeted tissues

#### *TRACER Capsid Discovery*

Our scientists have developed TRACER, a proprietary AAV capsid discovery platform to facilitate the selection of TRACER capsids for particular therapeutic applications based on BBB-crossing and cell-specific transduction properties in multiple species, including non-human primates, or NHPs. In May 2021, we presented data demonstrating that we have developed a series of TRACER capsids which, following intravenous administration, could achieve up to 1000-fold higher RNA expression in the brain and 100-fold higher expression in the spinal cord of NHPs than AAV9, the current natural AAV serotype with the best ability to cross the BBB. We also identified a TRACER capsid which displayed strong cardiac transduction and significant dorsal root ganglia de-targeting in NHPs, which may avoid toxicities associated with AAV9 delivery. We believe these TRACER capsids may allow for significantly enhanced gene delivery to specific types of cells in the brain at lower doses and, potentially, with fewer safety and tolerability issues than first-generation therapies. These TRACER capsids are now in advanced stages of characterization for deployment in our gene therapy development programs. We are also applying the TRACER discovery platform towards further capsid variant libraries and the selection for tropism and transduction in additional cell and tissue types.

At the American Society of Gene & Cell Therapy 25<sup>th</sup> Annual Meeting in May 2022, we presented new preclinical data on several families of TRACER capsids. We presented preclinical results for an AAV9-derived TRACER capsid, VCAP-102, which demonstrated 50-fold better transduction in mice and 60-fold better transduction in NHPs, compared to conventional AAV9 capsids, following intravenous administration. We believe demonstrating equivalent cross-species functionality is important to increasing a capsid's potential for translation into humans. The study also demonstrated that VCAP-102 and other TRACER capsids showed preferential tropism for glial cells in mice, which may facilitate addressing CNS indications that would benefit from non-neuronal cell transduction. We also presented preclinical data for an AAV5-derived TRACER capsid with enhanced CNS transduction across species. AAV5 capsids have a reduced prevalence of preexisting neutralizing antibodies, but conventional AAV5 capsids do not have sufficient CNS transduction to be used effectively for gene therapies targeting the CNS. Our AAV5-derived TRACER capsid showed 20-fold higher brain transduction and five-fold higher spinal cord transduction compared to conventional AAV9 in NHPs and improved transduction in multiple CNS regions and cell types in NHPs with partial de-targeting of the dorsal root ganglia.

We continue to perform screening campaigns with our TRACER discovery platform to identify additional proprietary AAV9- and AAV5-derived TRACER capsids and to refine previously-identified TRACER capsids to target or de-target multiple tissue and cell types. These TRACER capsids offer the potential to broaden the therapeutic window substantially and enable gene therapies in a wide range of diseases based on enhanced tissue and cell tropisms that allow for lower doses and with lower off-target effects or toxicities. We are currently conducting studies to assess gene expression and therapeutic indices at order-of-magnitude lower doses, and we intend to submit the results of these studies for presentation at an upcoming scientific conference.

We have identified the cell surface attachment receptor used by one of our more promising BBB-penetrant TRACER capsids. In addition to demonstrating direct binding to the human isoform of this receptor, our experiments have demonstrated that overexpression of human, murine, or cyno-derived orthologs of this receptor mediate improved transduction with AAV, supporting a conserved cross-species mechanism of action of transduction of this BBB-penetrant TRACER capsid. Further, the specificity of this AAV:receptor interaction is supported by experiments demonstrating that pharmacological manipulation of the receptor functionally impacts cellular transduction by the capsid, and that inhibition of the receptor's natural processing pathway blocks transduction. Expression of this receptor has been confirmed in rodent, NHP, and human endothelial cells and multiple CNS cell types. Accordingly, we believe that the characterization of this receptor and confirmation that those capsids can bind to the human isoform of the receptor increases the probability that the TRACER capsid will cross the BBB in humans. We expect the discovery of this receptor to support the clinical translatability of this TRACER capsid toward human application, and inform our approach to the design of future TRACER capsids for intravenous delivery. We also intend to explore whether this

receptor has the potential to enable intravenous delivery to the CNS for other therapeutic modalities such as proteins, antibodies, and oligonucleotides. We expect to share data on this finding at an upcoming scientific conference.

We are actively engaged in discussions to make TRACER capsids available to third parties for use in their drug development programs through potential licensing and other arrangements. We believe there is significant opportunity for out-licensing transactions related to our TRACER capsids. To maximize the potential of our TRACER capsids for both our own programs and out-licensing transactions, we have retained to date, and expect to retain in the future, all rights associated with such TRACER capsids other than the rights specific to their use in combination with the licensee's transgenes.

#### *Pfizer Option and License Agreement*

In October 2021, we entered into the Pfizer License Agreement, pursuant to which we have granted Pfizer options to receive an exclusive license, or the Pfizer License Options, to certain TRACER capsids to develop and commercialize certain AAV gene therapy candidates comprised of a capsid and specified Pfizer transgenes, which we refer to as the Pfizer Transgenes. Under the terms of the Pfizer License Agreement, Pfizer intends to evaluate the potential use of the capsids in combination with up to two Pfizer Transgenes to help treat respective central nervous system and cardiovascular diseases.

Under the Pfizer License Agreement, we have agreed to provide Pfizer with certain quantities of materials encoding specified existing capsids for Pfizer's evaluation. During the research term, which extends until October 1, 2022, or, in the event Pfizer exercises a Pfizer License Option, until October 1, 2024, we may, at our sole discretion and expense, conduct additional research activities to identify additional proprietary capsids that may be useful for AAV gene therapies for the treatment of central nervous system or cardiovascular diseases. We have agreed to disclose to Pfizer, on a rolling basis, the performance characteristics identified during the research term for all such capsid candidates. Following such disclosure, Pfizer has the right, in its sole discretion, to select any capsid candidate for evaluation to determine its interest in exercising a Pfizer License Option with respect to such capsid candidate. Pfizer may exercise up to two Pfizer License Options, provided that it may exercise only one Pfizer License Option for each Pfizer Transgene. We have granted Pfizer, effective upon Pfizer's exercise of a Pfizer License Option, with respect to a capsid candidate for the Pfizer Transgene identified therein, an exclusive, worldwide license, with the right to sublicense, under certain of our intellectual property, the rights to develop and commercialize the applicable licensed capsid as incorporated into products containing the corresponding Pfizer Transgene, or the Pfizer Licensed Products. Additionally, upon such option exercise, we and Pfizer have agreed that we shall provide certain additional know-how that has not been previously provided to Pfizer to enable Pfizer to exploit such licensed capsid and the corresponding Pfizer Transgene for use in a Pfizer Licensed Product. Pfizer may, during the research term, conduct additional evaluation of capsid candidates and has the right to substitute any other capsid candidate for the capsid it previously elected to license.

#### *Novartis Option and License Agreement*

In March 2022, we entered into the Novartis License Agreement, pursuant to which we have granted Novartis options, which we refer to as the Novartis License Options, to license novel capsids generated from our TRACER discovery platform, or Novartis Licensed Capsids, for exclusive use with certain targets to develop and commercialize adeno-associated virus gene therapy candidates comprised of Novartis Licensed Capsids and payloads directed to such targets, or the Novartis Payloads.

During the period, which we refer to as the Novartis Research Term, commencing on the Novartis Effective Date and ending on the first anniversary thereof or, in the event Novartis exercises a Novartis License Option, the third anniversary thereof, we have granted Novartis a non-exclusive research license to evaluate our TRACER capsids for potential use, in combination with Novartis Payloads, in programs targeting three specified genes, which we refer to as the Initial Novartis Targets. Upon the payment of additional fees, Novartis may also assess our TRACER capsids for use with two other targets, which we refer to as Additional Novartis Targets, subject to certain conditions including that such target is not part of, or reasonably competitive with, our current development programs. We refer to the Initial Novartis Targets and the Additional Novartis Targets, collectively, as the Novartis Targets. During the Novartis Research Term, we may, at our sole discretion and expense, conduct further research activities to identify additional TRACER capsids.



If we elect to do so, we have agreed to disclose performance characteristics of such new TRACER capsids to Novartis on a rolling basis.

During the Novartis Research Term, Novartis may exercise up to three Novartis License Options—or up to five Novartis License Options if Novartis is evaluating the Additional Novartis Targets—in the aggregate, provided that Novartis may only exercise one Novartis License Option for each Novartis Target. Upon the exercise of any Novartis License Option, we have agreed to grant Novartis a target-exclusive, worldwide license, with the right to sublicense, under certain of our intellectual property, the rights to develop and commercialize the applicable Novartis Licensed Capsid as incorporated into products containing the corresponding Novartis Payload, or the Novartis Licensed Products. Upon the exercise of a Novartis License Option, we have agreed to provide certain additional know-how to enable Novartis to exploit the Novartis Licensed Capsid and the corresponding Novartis Payload for use in a Novartis Licensed Product. Novartis may, during the Novartis Research Term but following the exercise of a Novartis License Option, conduct additional evaluation of our capsid candidates and has the right to substitute any other TRACER capsid for a Novartis Licensed Capsid.

#### *Neurocrine Collaboration*

In January 2019, we entered into the Neurocrine Collaboration Agreement for the research, development and commercialization of four programs including the VY-AADC Program, a gene therapy for the treatment of Friedreich's ataxia, or the FA Program, and other undisclosed programs, or the Discovery Programs. The Neurocrine Collaboration Agreement became effective in March 2019. Under the terms of the Neurocrine Collaboration Agreement, we received an upfront payment of \$115.0 million and may receive future development and regulatory milestone payments 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 collaboration agreement that we entered into with Genzyme Corporation in February 2015, we transferred ex-U.S. rights to the FA Program to Neurocrine pursuant to an amendment to the Neurocrine Collaboration Agreement and received a \$5.0 million payment from Neurocrine. Neurocrine is responsible for all costs incurred by us in conducting development activities for programs under the Neurocrine Collaboration Agreement, in accordance with an agreed budget.

#### *Anti-Tau Antibody Program for the Treatment of Alzheimer's Disease*

We are developing proprietary antibodies that selectively target pathological tau to treat tauopathies. Our lead indication for these antibodies is Alzheimer's disease. We have maintained a long-standing focus on developing proprietary and complimentary approaches to disrupt the progression of tau pathology believed to be central to Alzheimer's disease and other relevant neurodegenerative diseases. Reduction of toxic tau aggregates may slow disease progression and cognitive decline in these diseases. We are exploring both passive administration and vectorized delivery utilizing our BBB-penetrant TRACER capsids with our anti-tau antibody. Collectively, our passive and vectorized anti-tau antibodies have differentiated properties including improved targeting of specific regions of tau protein that could offer an improved profile compared to first-generation approaches. We believe that our antibody targeting the C-terminus is highly differentiated from other approaches. Further, we believe that following the clearance of an investigational new drug, or IND, application, clinical assessments utilizing positron emission tomography (PET) imaging of human tau, together with measuring plasma and cerebrospinal fluid biomarkers, have the potential to enable an efficient and accelerated demonstration of human proof-of-biology.

At the Alzheimer's Association International Conference in August 2022, we presented data for our proprietary anti-tau antibodies, targeting the mid-domain and C-terminus with high affinity and showing favorable biophysical characteristics and strong activity in preclinical studies in mouse models. In the P301S seeding-propagation tauopathy mouse model, our C-terminal targeting anti-tau antibody blocked the seeding/propagation of filamentous tau and demonstrated substantial reduction of induced tau pathology.

Humanization of the murine antibody is currently underway. We intend to nominate a lead antibody development candidate in the first half of 2023, initiate Good Laboratory Practice, or GLP, toxicology studies in the second half of 2023, and, if preclinical results are supportive, file an IND application in the first half of 2024.

*GBA1 Gene Replacement Program for the Treatment of Parkinson's Disease*

We are developing a gene therapy leveraging a BBB-penetrant, CNS-tropic TRACER capsid to treat diseases linked to GBA1 mutations via a gene replacement approach. Our lead indication for this gene therapy is Parkinson's disease with GBA1 mutations. Mutations in GBA1, the gene encoding the lysosomal enzyme glucocerebrosidase, or GCase, are the most common genetic risk factor for synucleinopathies such as Parkinson's disease. Parkinson's disease is among the most common neurodegenerative diseases, impacting about one million patients in the United States and more than 10 million patients worldwide. Up to 10% of Parkinson's disease patients have a GBA1 mutation, and these mutations increase the risk of Parkinson's disease by approximately 20-fold. GBA1 mutations decrease the expression of GCase, leading to the accumulation of GCase substrates and alpha-synuclein aggregates, which is thought to be toxic to neurons.

We believe that restoring GCase activity may attenuate disease progression and potentially slow neurodegeneration. We anticipate delivering GBA1 via intravenous administration to enable widespread distribution to multiple affected brain regions and to avoid the need for more invasive approaches. We believe that the measurement of the GCase substrates such as glucosylsphingosine as cerebrospinal fluid biomarkers may facilitate efficient clinical demonstration of proof-of-biology. Such substrates of the GCase enzyme are elevated in the cerebrospinal fluid of Parkinson's disease patients who harbor the GBA1 mutation, and we expect that substrate levels would fall to normal if our gene therapy restores GCase enzyme expression in the brain. This gene therapy may also have potential utility in idiopathic Parkinson's disease, where there is evidence of loss of GCase activity in the substantia nigra in Parkinson's disease patients even in the absence of GBA1 mutations as well as evidence of lysosomal dysfunction in general.

At the American Society of Gene & Cell Therapy 25<sup>th</sup> Annual Meeting in May 2022, we presented preclinical data demonstrating CNS target engagement and delivery of therapeutically relevant levels of GCase in a GBA loss of function mouse model, as well as sustained expression for three or more months following intravenous administration.

An NHP capsid selection study for the program is currently underway. We intend to select a development candidate in the first half of 2023, initiate a dose range finding study in NHPs in the second half of 2023, initiate GLP toxicology studies in 2024, and if preclinical results are supportive, file an IND application in 2025. We are evaluating options to further accelerate the development timeline for this program.

*SOD1 Gene Silencing Program for the Treatment of ALS*

We are developing a gene therapy leveraging a BBB-penetrant, CNS-tropic TRACER capsid to treat ALS caused by the SOD1 mutation via a gene silencing approach. SOD1 ALS is typically fatal within approximately three years of diagnosis and impacts approximately 800 patients in the United States, 1,000 patients in the European Union, and 500 patients in Japan. SOD1 mutations in ALS patients are thought to cause a toxic gain-of-function that leads to the degeneration of motor neurons along the entire length of the spinal cord, the brainstem, and the upper motor neurons in the cerebral cortex. We believe that a therapeutic delivering a highly potent small interfering RNA, or siRNA, construct via intravenous administration may enable broad CNS knockdown of SOD1, potentially slowing the decline of functional ability in ALS patients with the SOD1 mutation. We believe that a Phase 1 clinical trial to demonstrate reduction in SOD1 in cerebrospinal fluid and neurofilament light chain in plasma will provide evidence of target engagement and the attenuation of motor neuron loss, respectively.

At the American Society of Gene & Cell Therapy 25<sup>th</sup> Annual Meeting in May 2022, we presented preclinical data demonstrating robust SOD1 knockdown in all levels of the spinal cord and significant improvements in motor performance, body weight, and survival in a SOD1-ALS mouse model following intravenous delivery of a vectorized siRNA using a mouse BBB-penetrant capsid.

Our NHP capsid selection study for the program is already underway, and we expect to select a development candidate for the program by the end of 2022. We intend to complete a dose range-finding NHP study in 2023, initiate GLP toxicology studies in the first half of 2024, and, if preclinical results are supportive, file an IND application in 2024.

*Other Discovery and Preclinical Pipeline Programs*

We are evaluating additional neurological and other diseases that could be treated using AAV gene therapy through application of either a gene replacement or a gene silencing approach and are also actively exploring additional potential treatment methods that can utilize an AAV vector. We expect to leverage our proprietary gene therapy platform technologies, including TRACER capsids and our vectorized antibody platform, for any such programs. We are pursuing additional product candidates in the discovery and preclinical stages of development, including a second-generation treatment program for Huntington's Disease and a treatment program for SMA, which leverage our TRACER capsids, and a treatment program for HER2+ brain metastases, which leverages a TRACER capsid and our vectorized antibody platform. We are evaluating opportunities to advance these programs via collaborative partnership, and will continue to conduct preclinical research for our second-generation program for the treatment of Huntington's disease and our program for the treatment of HER2+ brain metastases. We expect to continue to conduct early preclinical research for our second-generation program for the treatment of SMA as we seek a collaborative partner for the program.

*Vector Engineering and Optimization*

We have advanced or intend to advance our multiple preclinical programs towards selection of lead clinical candidates using AAV vectors that we believe are best suited for each of our programs either through use of our existing capsids, through exercising a non-exclusive worldwide commercial license to capsid sequences covered by third parties, or by engineering or optimizing TRACER capsids. The key components of an AAV vector include: (i) the capsid; (ii) the therapeutic gene, or transgene; and (iii) payload control elements, including the promoter or other DNA sequences that modulate the expression of the transgene.

We have a history of incurring significant losses. Our net loss was \$40.4 million for the six months ended June 30, 2022. As of June 30, 2022, we had an accumulated deficit of \$387.5 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;
- increase our investment in and support for TRACER, our proprietary discovery platform to facilitate the selection of AAV capsids and expand our investment to discover TRACER capsids with broad tropism in CNS and other tissues with cell-specific transduction properties for particular therapeutic applications;
- continue to develop our vectorized antibody platform and other proprietary antibodies;
- enter into licensing agreements regarding our TRACER capsids, such as the Pfizer License Agreement and the Novartis License Agreement;
- conduct preclinical development activities and initiate IND-enabling studies and clinical trials in connection with our tau antibody program, our GBA1 gene therapy program, and our SOD1 ALS gene therapy program;
- 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 diseases for treatment with our AAV gene therapies and develop additional programs or product candidates;
- seek marketing and regulatory approvals for any of our product candidates or devices 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;
- continue to operate as a public company; and
- determine the appropriate path forward, if any, for VY-AADC (NBIb-1817) as a treatment for Parkinson's disease.

## **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, 2022, we recognized \$1.4 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 the Neurocrine Collaboration Agreement, the Pfizer License Agreement, and the Novartis License Agreement, 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 the Neurocrine Collaboration Agreement, the Pfizer License Agreement, the Novartis License Agreement, and any other strategic collaborations and out-licensing arrangements 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, vectorized antibody platform, and proprietary antibodies, 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;

## [Table of Contents](#)

- 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:

- identifying additional product candidates;
- completing preclinical studies successfully;
- designing, initiating, enrolling and completing clinical trials successfully;
- establishing an appropriate safety profile;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- receiving 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
- recruiting and retaining key research and development personnel.

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

Research and development activities are central to our business model. We are in the early stages of development of our product candidates. Our research and development costs have decreased relative to pre-2021 levels as a result of our strategic restructuring, the reevaluation of our product candidate pipeline, our strategic shift to invest in TRACER capsid development efforts, and our initiation of other cost-saving initiatives. As our development programs progress and as we identify product candidates and initiate preclinical studies and clinical trials, we expect research and development costs to increase.

### 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.

Our general and administrative expenses have decreased relative to pre-2021 levels as a result of our strategic restructuring costs. As a result of the strategic restructuring, there are decreases including a reduction in personnel costs and fees paid to outside consultants, as well as other cost-saving initiatives including a reduction in facility-related expenditures. As our development programs progress and we identify product candidates and initiate preclinical studies and clinical trials, we expect general and administrative expenses to increase to support these additional research and development activities.

### Other Income (Expense), net

Other income (expense) for the three months ended June 30, 2022 consists primarily of interest income on our marketable securities. In the three months ended June 30, 2021 we recorded a gain on our investment in equity securities of ClearPoint Neuro, Inc. (formerly known as MRI Interventions, Inc.), or CLPT. All equity securities in CLPT held by us were sold or otherwise disposed of during the three months ended June 30, 2021.

### 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, 2022, as compared to those identified in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021. 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 8, 2022.

### Results of Operations

#### Comparison of the three months ended June 30, 2022 and 2021

The following table summarizes our results of operations for the three months ended June 30, 2022 and 2021, together with the changes in those items in dollars:

	Three Months Ended		
	June 30,		Change
	2022	2021	
	<i>(in thousands)</i>		
Collaboration revenue	\$ 712	\$ 1,357	\$ (645)
Operating expenses:			
Research and development	12,527	19,505	(6,978)
General and administrative	7,552	10,437	(2,885)
Total operating expenses	<u>20,079</u>	<u>29,942</u>	<u>(9,863)</u>
Other income, net:			
Interest income	219	48	171
Other (expense) income	61	(1,583)	1,644
Total other income	<u>280</u>	<u>(1,535)</u>	<u>1,815</u>
Net (loss) income	<u>\$ (19,087)</u>	<u>\$ (30,120)</u>	<u>\$ 11,033</u>

### Collaboration Revenue

Collaboration revenue was \$0.7 million and \$1.4 million for the three months ended June 30, 2022 and 2021, respectively. The decrease in collaboration revenue in the three months ended June 30, 2022 was largely a result of our reduced research and development services related to the Neurocrine Collaboration as a result of Neurocrine's termination of the Neurocrine Collaboration Agreement with respect to the VY-AADC Program. During the three months ended June 30, 2022 and June 30, 2021, collaboration revenue was entirely related to research services and cost reimbursement from the Neurocrine Collaboration. As a result of changes in our estimates of research and development services in the fourth quarter of 2021, we expect to record less revenue associated with research and development services for the Neurocrine Collaboration. We expect a significant portion of revenue recognized in future periods to be attributable to the Pfizer License Agreement and the Novartis License Agreement. Our collaboration revenues were not materially impacted by the coronavirus disease 2019, or COVID-19, pandemic during the three months ended June 30, 2022. In subsequent periods, the COVID-19 pandemic could affect our collaboration revenues and our operations.

### Research and Development Expense

Research and development expense decreased by \$7.0 million from \$19.5 million for the three months ended June 30, 2021, to \$12.5 million for the three months ended June 30, 2022. The following table summarizes our research and development expenses for the three months ended June 30, 2022 and 2021, together with the changes in those items in dollars:

	Three Months Ended		Change
	June 30,		
	2022	2021	
	<i>(in thousands)</i>		
Employee and consultant	\$ 6,924	\$ 10,265	\$ (3,341)
External research and development	2,794	4,283	(1,490)
Facilities and other	1,022	2,458	(1,437)
Professional fees	1,787	2,498	(711)
Total research and development expenses	<u>\$ 12,527</u>	<u>\$ 19,505</u>	<u>\$ (6,978)</u>

The decrease in research and development expense for the three months ended June 30, 2022 was primarily attributable to the following:

- approximately \$1.5 million for external research and development costs primarily related to a reduction in clinical activities to prepare for the first-in humans trial of the VY-HTT01 for the Huntington's disease program; and
- approximately \$3.3 million for employee and consultant related costs associated with lower headcount in research and development functions as compared to the prior year; and
- approximately \$1.4 million for decreased facility and other costs primarily related to the gain recorded on the terminated lease at 75 Sidney as disclosed in this Quarterly Report on Form 10-Q.
- approximately \$0.7 million for decreased professional fees and related expenses to support the pipeline programs.

### General and Administrative Expense

General and administrative expense decreased by \$2.8 million from \$10.4 million for the three months ended June 30, 2021 to \$7.6 million for the three months ended June 30, 2022. The increase in general and administrative expense was primarily attributable to the following:

- approximately \$1.6 million for decrease compensation costs and stock-based compensation associated with recognition of the severance expensed as a result of the reduction in force;
- approximately \$0.9 million for decreased facility and other costs primarily related to the gain recorded on the terminated lease at 75 Sidney as disclosed in this Quarterly Report on Form 10-Q; and
- approximately \$0.3 million for decreased legal costs and intellectual property related expenses..

### Other (Expense) Income, net

Interest and other income of approximately \$280 thousand and interest and other expense of approximately \$1.5 million was recognized during the three months ended June 30, 2022 and 2021, respectively. Other income during the three months ended June 30, 2022 primarily related to interest income on marketable securities balances, while other income during the three months ended June 30, 2021 primarily related to a gain on our investment in equity securities of CLPT. All equity securities in CLPT held by us were sold or otherwise disposed of during the three months ended June 30, 2021.

### Comparison of the six months ended June 30, 2022 and 2021

The following table summarizes our results of operations for the six months ended June 30, 2022 and 2021, together with the changes in those items in dollars:

	Six Months Ended		Change
	June 30,		
	2022	2021	
	<i>(in thousands)</i>		
Collaboration revenue	\$ 1,371	\$ 7,858	\$ (6,487)
Operating expenses:			
Research and development	26,876	41,851	(14,975)
General and administrative	15,211	20,181	(4,970)
Total operating expenses	42,087	62,032	(19,945)
Other income, net:			
Interest income	271	132	139
Other income (expense)	39	2,273	(2,234)
Total other income, net	310	2,405	(2,095)
Net (loss) income	\$ (40,406)	\$ (51,769)	\$ 11,363

### Collaboration Revenue

Collaboration revenue was \$1.4 million and \$7.9 million for the six months ended June 30, 2022 and 2021, respectively. The decrease in collaboration revenue in the three months ended June 30, 2022 was largely a result of our reduced research and development services related to the Neurocrine Collaboration as a result of Neurocrine's termination of the Neurocrine Collaboration Agreement with respect to the VY-AADC Program. During the three months ended June 30, 2022 and June 30, 2021, collaboration revenue was entirely related to research services and cost reimbursement from the Neurocrine Collaboration. As a result of changes in our estimates of research and development services in the fourth quarter of 2021, we expect to record less revenue associated with research and development services for the Neurocrine Collaboration. We expect a significant portion of revenue recognized in future periods to be



attributable to the Pfizer License Agreement and the Novartis License Agreement. Our collaboration revenues were not materially impacted by the coronavirus disease 2019, or COVID-19, pandemic during the three months ended June 30, 2022. In subsequent periods, the COVID-19 pandemic could affect our collaboration revenues and our operations.

*Research and Development Expense*

Research and development expense decreased by \$15.0 million from \$41.9 million for the six months ended June 30, 2021, to \$26.9 million for the six months ended June 30, 2022. The following table summarizes our research and development expense, for the six months ended June 30, 2022 and 2021:

	Six Months Ended		
	June 30,		
	2022	2021	Change
	<i>(in thousands)</i>		
Employee and consultant	\$ 13,567	\$ 21,690	\$ (8,124)
External research and development	4,595	10,347	(5,752)
Facilities and other	4,627	4,976	(349)
Professional fees	4,088	4,837	(749)
Total research and development expenses	<u>\$ 26,876</u>	<u>\$ 41,851</u>	<u>\$ (14,974)</u>

The decrease in research and development expense for the six months ended June 30, 2022 was primarily attributable to the following:

- approximately \$5.8 million for external research and development costs primarily related to a reduction in clinical and manufacturing activities to prepare for the first-in humans trial of the VY-HTT01 for the Huntington’s disease and decrease spend on external costs incurred in connection with the Neurocrine Collaboration Agreement; and
- approximately \$8.1 million for employee and stock-based compensation associated with lower headcount in research and development functions compared to the prior year; and
- approximately \$0.3 million of decreased facility and other costs primarily related to the gain recorded on the terminated lease at 75 Sidney as disclosed in this Quarterly Report on Form 10-Q, partially offset by increased facility and other costs including rent, depreciation, maintenance, and other expenses.
- Approximately \$0.8 million for decreased professional fees and related expenses to support the pipeline programs.

*General and Administrative Expense*

General and administrative expense decreased by \$5.0 million from \$20.2 million for the six months ended June 30, 2021 to \$15.2 million for the six months ended June 30, 2022. The decrease in general and administrative expense was primarily attributable to the following:

- approximately \$3.1 million for decreased compensation costs and stock-based compensation associated with recognition of the severance expensed as a result of the reduction in force;
- approximately \$0.8 million for decreased facility and other costs primarily related to the gain recorded on the terminated lease at 75 Sidney Street; and
- approximately \$1.1 million for decreased legal costs and intellectual property related expenses.

### *Other Income, net*

Interest and other income of approximately \$310 thousand and \$2.4 million were recognized during the six months ended June 30, 2022 and 2021, respectively. Other income during the six months ended June 30, 2022 relates to interest income on marketable securities balances, while other income the six months ended June 30, 2021 primarily related to a gain on our investment in equity securities of CLPT. All equity securities in CLPT held by us were sold or otherwise disposed of during the six months ended June 30, 2021.

### **COVID-19**

The COVID-19 pandemic continues to evolve. We have and will continue to be guided by applicable guidelines and safety measures, including any stay-at-home policies for certain non-essential employees, consultants, contractors, and staff. Certain of our clinical trial sites, collaboration partners, suppliers and consultants have experienced facility closures or been subject to quarantines, travel restrictions and other governmental restrictions or supply chain disruptions 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.

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.

### **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, our strategic collaborations, including our prior Sanofi Genzyme Collaboration, AbbVie Tau Collaboration, and AbbVie Alpha-Synuclein Collaboration, our ongoing Neurocrine Collaboration, and our out-licensing arrangements, including the Pfizer License Agreement and the Novartis License Agreement.

As of June 30, 2022, we had cash, cash equivalents, and marketable securities of \$148.1 million. Based upon our current operating plans, we expect that our existing cash, cash equivalents, and marketable securities at June 30, 2022, together with amounts expected to be received as reimbursement for development costs under the Neurocrine Collaboration Agreement, will enable us to meet our planned operating expenses and capital expenditure requirements into 2024.

#### *Cash Flows*

The following table provides information regarding our cash flows for the six months ended June 30, 2022 and 2021:

	<b>Six Months Ended</b>	
	<b>June 30,</b>	
	<b>2022</b>	<b>2021</b>
	<i>(in thousands)</i>	
Net cash (used in) provided by:		
Operating activities	\$ 15,941	\$ (44,011)
Investing activities	(56,128)	57,030
Financing activities	819	385
Net (decrease) increase in cash, cash equivalents, and restricted cash	<u>\$ (39,368)</u>	<u>\$ 13,404</u>

*Net Cash Provided by (Used in) Operating Activities*

Net cash provided by operating activities was \$15.9 million during the six months ended June 30, 2022 compared to \$44.0 million of net cash used in operating activities during the six months ended June 30, 2021. The cash provided by operating activities for the six months ended June 30, 2022 compared to the cash used in operating activities for the six months ended June 30, 2021 was primarily due to an upfront payment of \$54.0 million received pursuant to the Novartis License Agreement in March 2022.

*Net Cash Used in (Provided by) Investing Activities*

Net cash used in investing activities was \$56.1 million during the six months ended June 30, 2022 compared to \$57.0 million of net cash provided by investing activities during the six months ended June 30, 2021. The net cash used in investing activities for the six months ended June 30, 2022 was primarily due to \$54.8 million for purchases of marketable securities and \$1.3 million for purchases of property and equipment. The net cash provided by investing activities for the six months ended June 30, 2021 was primarily due to proceeds of \$57.6 million from sales and maturities of marketable securities partially offset by \$0.6 million for purchases of property and equipment.

*Net Cash Provided by Financing Activities*

Net cash provided by financing activities was \$0.8 million and \$0.4 million during the six months ended June 30, 2022 and June 30, 2021, respectively, primarily due to the proceeds from the exercise of stock options.

*Funding Requirements*

We expect our expenses to decrease from prior year in the near term as a result of our strategic restructuring, the reevaluation of our product candidate pipeline, our strategic shift to invest in TRACER capsid development efforts, and our initiation of other cost-saving initiatives. We expect our expenses to increase in the future, however, as we continue the research and development of, conduct clinical trials of, and seek marketing approval for, our product candidates and as we continue to enter into or conduct activities in connection with 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 securities at June 30, 2022, together with amounts expected to be received as reimbursement for development costs under the Neurocrine Collaboration Agreement, will be sufficient to meet our planned operating expenses and capital expenditure requirements into 2024. 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;
- the scope, progress, results, costs, prioritization, and number of our research and development programs;
- the progress and status of our strategic collaborations and licensing agreements, including any research and development costs for which we are responsible, our collaborators' or licensors' willingness and ability to approve desirable budgets for research and development costs for which they are responsible, the potential exercise by our collaboration partners or licensors of any options to develop or license certain products and product candidates that they might have, our potential receipt of future milestone payments and royalties

from our collaboration partners or licensors, and any decisions by our collaborators or licensors to exercise their rights to terminate a collaboration in whole or in part;

- 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, acquire or invest in other businesses, or out-license our product candidates, capsids or other technologies;
- 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 consistent 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 and licensors for reimbursement of certain research and development expenses, potential option exercises, the achievement of specified regulatory and commercial milestones, and royalty payments under our collaboration and licensing agreements, as applicable. 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***

We enter into agreements in the normal course of business with clinical research organizations, contract manufacturing organizations, and institutions to license intellectual property. These contracts are generally cancelable at any time by us, upon 30 to 90 days prior written notice.

Our agreements to license intellectual property include potential milestone payments that are dependent upon the development of products using the intellectual property licensed under the agreements and contingent upon the achievement of clinical trial or regulatory approval milestones. We may also be required to pay annual maintenance fees or minimum amounts payable ranging from low-four digits to low five-digits depending upon the terms of the applicable agreement.

We also have non-cancelable operating lease commitments arising from our leases of office and laboratory space at our facilities in Cambridge and Lexington, Massachusetts.

Other than the termination of our lease for 75 Sidney Street, as discussed elsewhere in this Quarterly Report on Form 10-Q, 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, 2021, as filed with the SEC on March 8, 2022.

### **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.

## **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, 2022.

## **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, 2022. 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, 2022, 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, 2022, 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**

In the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation relating to intellectual property, commercial arrangements and other matters. While the outcome of these proceedings and claims cannot be predicted with certainty, as of June 30, 2022, we were not party to any legal matters, claims, or arbitration proceedings that may have, or have had in the recent past, significant effects on our financial position or profitability. No governmental proceedings are pending or, to our knowledge, contemplated against us. We are not a party to any material proceedings in which any director, member of senior management or affiliate of ours is either a party adverse to us or our subsidiaries or has a material interest adverse to us or our subsidiaries.

### **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 a history of incurring significant losses and anticipate that we will continue to incur losses for the foreseeable future and may never achieve or maintain consistent profitability.*

We are an early-stage gene therapy company with a limited operating history and have not yet generated revenues from the sales of our product candidates. All of our product candidates are in the early stages of development. 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. We have a history of incurring significant operating losses. Our net losses were \$40.4 million and \$51.8 million for the six months ended June 30, 2022 and June 30, 2021, respectively. As of June 30, 2022, we had an accumulated deficit of \$387.5 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 our prior collaborations with Sanofi Genzyme Corporation, or Sanofi Genzyme, and AbbVie, and our ongoing collaboration with Neurocrine Biosciences, Inc., or Neurocrine, our option and license agreement with Pfizer Inc., or Pfizer, which commenced in October 2021, and our option and license agreement with Novartis Pharma, AG, or Novartis, which commenced in March 2022. We refer to the Pfizer option and license agreement as the Pfizer License Agreement, and to the Novartis option and license agreement as the Novartis License Agreement.

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.

Although our expenses have decreased relative to pre-2021 as a result of our strategic restructuring, the reevaluation of our product candidate pipeline, and our strategic shift to invest in TRACER capsid development efforts, 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;
- increase our investment in and support for TRACER™ (Tropism Redirection of AAV by Cell Type-Specific Expression of RNA), our proprietary discovery platform to facilitate the selection of AAV capsids and expand our investment to discover TRACER capsids with broad tropism in central nervous system, or CNS and other tissues with cell-specific transduction properties for particular therapeutic applications;
- continue to develop our vectorized antibody platform and other proprietary antibodies;
- enter into licensing agreements regarding our TRACER capsids, such as the Pfizer License Agreement and the Novartis License Agreement;
- conduct preclinical development activities and initiate investigational new drug, or IND, application-enabling studies and clinical trials in connection with our tau antibody program, our GBA1 gene therapy program, and our SOD1 ALS gene therapy program;

## [Table of Contents](#)

- 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 diseases for treatment with our AAV gene therapies and develop additional programs or product candidates;
- seek marketing and regulatory approvals for any of our product candidates or devices 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;
- continue to operate as a public company; and
- determine the appropriate path forward, if any, for VY-AADC (NBIB-1817) as a treatment for Parkinson's disease.

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 consistent 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
- 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 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 include completing preclinical studies and clinical trials of our product candidates; obtaining marketing approval for these product candidates; contracting with third parties with expertise in current good manufacturing practice, or cGMP, manufacturing to manufacture our product candidates 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 consistently 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. All of our product candidates are in the early stages of development. We do not anticipate generating revenues from product sales for at least 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 and licensors' success in:

- completing preclinical and clinical development of our product candidates or product candidates incorporating our licensed capsids or other technologies and identifying new product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we or they complete clinical trials;
- launching and commercializing product candidates for which we or they 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 or their product candidates, if and when approved;
- obtaining an adequate level of market acceptance of our or their 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.***

Although our expenses have decreased relative to pre-2021 levels as a result of our strategic restructuring, the reevaluation of our product candidate pipeline, and our strategic shift to invest in TRACER capsid development efforts, we expect our expenses to increase over time 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, 2022, our cash, cash equivalents, and marketable securities were \$148.1 million. Based upon our current operating plan, we expect that our existing cash, cash equivalents, and marketable securities at June 30, 2022, together with amounts expected to be received as reimbursement for development costs under 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 2024.

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;
- the scope, progress, results, costs, prioritization, and number of our research and development programs;
- the progress and status of our strategic collaborations and licensing agreements, including any research and development costs for which we are responsible, our collaborators' or licensors' willingness and ability to approve desirable budgets for research and development costs for which they are responsible, the potential exercise by our collaboration partners or licensors of any options to develop or license certain products and product candidates that they might have, our potential receipt of future milestone payments and royalties from our collaboration partners or licensors, and any decisions by our collaborators or licensors to exercise their rights to terminate a collaboration in whole or in part;
- 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, acquire or invest in other businesses, or out-license our product candidates, capsids or other technologies;
- 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 maintain the financial support of our collaborators or obtain marketing approval and achieve product sales. In the event we are unable to achieve milestones necessary to demonstrate progress on those programs, a current or future collaboration partner or licensor may be unwilling to fund these programs at the desired levels or at all, which could require us to fund these programs to a greater extent than we have expected, to decline to pursue certain program objectives or to discontinue one or more of the programs. Our ability to develop a product candidate for any of our lead gene therapy or antibody programs may take longer than we anticipate, or may not happen at all, and could require funding at a level higher than we expect. Our product revenues, if any, and any commercial milestone payments or royalty payments under our collaboration or licensing agreements will be derived from sales of products that may not be commercially available for many years, if at all. In addition, our product candidates, if approved, may not achieve commercial success. 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 consistent 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 partner Neurocrine for the reimbursement of certain research and development expenses, the achievement of specified regulatory and commercial milestones, and royalty payments under our collaboration agreement and the amounts we are entitled to receive from our licensors Pfizer and Novartis for the achievement of specified development, regulatory, and commercialization milestones and royalty payments under the applicable option and license 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. The amount of stockholder dilution will be affected by the size of each securities offering and the offering price for the securities sold. The offering price will likely reflect the prevailing market price for our securities, with dilution increasing as the prevailing market price for our securities decreases. 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.***

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 early-phase 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 such as the regulatory actions that previously occurred in connection with the VY-AADC Program for Parkinson's disease and the VY-HTT01 Program for Huntington's disease. These and other events that are part of our operating history, and ongoing activities such as our decision to conduct a reevaluation of our product candidate pipeline and to restructure our workforce, may impact our ability to operate our business and to raise capital. All of our product candidates are in the early stages of development. 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 and antibody product candidates are based on a proprietary technology and, in several disease areas, unvalidated treatment approaches, 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. We currently only have one product candidate, VY-AADC (NB1b-1817), which has entered clinical development, and the RESTORE-1 Phase 2 clinical trial in which VY-AADC (NB1b-1817) is being evaluated is on clinical hold. Our collaboration partner Neurocrine is the study sponsor and IND holder for the VY-AADC program, and it terminated its participation in the program, effective August 2, 2021.

We determined in 2021 that we would not advance the VY-AADC program unless the program is partnered with another collaborator. 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. Additionally, 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 an AAV gene therapy product. Since that time, it has approved a limited number of gene therapy products including Luxturna, an AAV gene therapy product by Spark Therapeutics, Inc. (acquired by F. Hoffmann-La Roche Ltd., or Roche, in 2019), or 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. In Europe, a similarly limited number of AAV gene therapy products including Luxturna and Zolgensma, as well as Glybera by uniQure N.V., or uniQure, 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.

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 (NB1b-1817), the PD-1102 Phase 1 trial exploring the delivery of VY-AADC (NB1b-1817) using a posterior trajectory, and the RESTORE-1 Phase 2 clinical trial were conducted at multiple sites, and therefore are subject to oversight by these authorities. If the protocol for such a trial was amended, it would need to be re-reviewed by the respective institutional IRBs of each institution. 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, in connection with the RESTORE-1 Phase 2 clinical trial, we and our collaboration partner Neurocrine paused screening of new patients, in part to facilitate IRB reviews of certain amendments made to the clinical trial protocol. As the FDA imposed a clinical hold on the RESTORE-1 Phase 2 clinical trial in December 2020, the resumption of any patient screening or dosing in the trial is now subject to the resolution of the clinical hold currently in effect.

Adverse or unforeseen 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. For example, we requested feedback from the FDA on, among other matters, the regulatory pathway for VY-AADC (NBIB-1817) and the design of the 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). 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.

In connection with our Neurocrine Collaboration Agreement, we agreed to transfer sponsorship of the clinical research program for VY-AADC (NBIB-1817) in Parkinson's disease, or the VY-AADC Program, to Neurocrine, which required the related IND application to be transferred to Neurocrine. The transition process required additional regulatory filings with and review by the FDA. Based upon feedback received from the FDA, we and Neurocrine amended the RESTORE-1 clinical trial protocol. Following Neurocrine's termination of the Neurocrine Collaboration Agreement with respect to the VY-AADC Program, Neurocrine remains the sponsor of the RESTORE-1 Phase 2 clinical trial and the holder of the applicable IND. If sponsorship of the RESTORE-1 Phase 2 clinical trial is transferred back to us at our request, such transition would require additional regulatory filings with and review by the FDA, and would likely lead to additional costs and delays in the enrollment of patients in any potential future clinical trials we or a collaboration partner would pursue in connection with the VY-AADC Program.

In October 2020, the FDA notified us that the IND application for our planned Phase 1/2 clinical trial to evaluate VY-HTT01 in patients with Huntington's disease was placed on clinical hold pending the resolution of certain information requests regarding chemistry, manufacturing, and controls, or CMC, matters. We had 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, however, we were unable to have additional formal consultations with the FDA prior to our submission of our IND application in September 2020 concerning changes to the program since our 2017 meeting. Although we resolved the clinical hold, we decided in August 2021 not to commence the VYTAL Phase 1/2 clinical trial for VY-HTT01 and to pursue the development of a second-generation program for the treatment of Huntington's disease using a novel, proprietary AAV capsid to enable enhanced transduction and broad distribution with intravenous administration. These and other regulatory delays may require us to incur additional clinical development costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue from our product candidates.

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. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of increased or lengthier regulatory approval process and further restrictions on development of our product candidates can be costly and could negatively impact our or our

collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

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

All of our product candidates are in early stages of development, and the risk of failure is high. 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. For example, data from the PD-1101 Phase 1b clinical trial and from the separate PD-1102 Phase 1 clinical trial exploring the delivery of VY-AADC (NB1b-1817) using a posterior trajectory suggest that one-time treatment with VY-AADC (NB1b-1817) could result in sustained improvement in motor function in patients with Parkinson's disease. These results, however, may not be predictive of the results of the RESTORE-1 Phase 2 clinical trial or any future clinical trials that we or a collaboration partner could choose to conduct on VY-AADC (NB1b-1817). Some of our clinical trials, including the PD-1101 and PD-1102 clinical trials, 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.

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

To date, we have only conducted clinical trials in the United States. However, we may in the future choose to conduct one or more of our clinical trials or include sites in current or future clinical trials outside the United States.

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;
- the 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;
- the 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 are early in our development efforts. Our primary product candidates are in the discovery and preclinical stages of development. 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.***

We are early in our development efforts, and our primary product candidates are in preclinical development. 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. Our ability to complete our preclinical testing and studies is contingent on our ability to source animals and other supplies required for the conduct of such testing and studies. If we are unable to obtain all necessary animals and other supplies required for the conduct of our preclinical testing and studies, we may be unable to complete such preclinical testing and studies in a timely manner or at all. For example, some of our IND-enabling toxicology and other studies require certain non-human primates that are customarily imported from the People's Republic of China, or the PRC, and current trade relations between the United States and the PRC has made the sourcing of these non-human primates challenging. We have encountered, and may continue to encounter, delays in obtaining a sufficient supply of such non-human primates to enable the conduct of our preclinical studies and testing. In addition, we may need to conduct preclinical studies utilizing non-human primates located in testing facilities outside of the United States. Utilizing such facilities will require us to observe export control regulations for the shipment of vectors and transgenes and import controls for the shipment of samples to us for evaluation and storage, which controls we may not be to satisfy, or may result in delay or additional expense. Our inability to obtain access to a sufficient supply of these non-human primates in a timely manner or at all may impair our ability to complete preclinical testing and studies to support IND applications or similar applications in other jurisdictions or delay the submission of such applications.

Additionally, we 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.

For example, in September 2020, we submitted an IND to the FDA in connection with the proposed initiation of a planned Phase 1/2 clinical trial for VY-HTT01 in patients with Huntington's disease. In October 2020, the FDA notified us that the IND application for VY-HTT01 was placed on clinical hold pending the resolution of certain CMC information requests. We provided a complete response to the additional requests from the FDA regarding the IND application for VY-HTT01 in the first quarter of 2021, and the FDA removed its clinical hold on the IND and confirmed that we could proceed with our planned VYTAL Phase 1/2 clinical trial in April 2021. Although we resolved the clinical hold, we decided in August 2021 not to initiate our planned VYTAL Phase 1/2 clinical trial. This delay and our subsequent decision to refocus our program for the treatment of Huntington's disease on the development of a second-



generation product candidate could increase our expenses and adversely impact our ability to commercialize a product candidate for the treatment of Huntington's disease in a timely manner, if at all.

We also have very limited experience with clinical trials. The transfer of sponsorship of the VY-AADC Program to Neurocrine required Neurocrine to become the sponsor of the RESTORE-1 Phase 2 clinical trial in many sites. The sponsorship transition required additional regulatory filings with and review by regulatory officials, and led to additional costs and delays in the enrollment of patients in the RESTORE-1 Phase 2 clinical trial. Following Neurocrine's termination of the Neurocrine Collaboration Agreement with respect to the VY-AADC Program, Neurocrine remains the sponsor of the RESTORE-1 Phase 2 clinical trial and the holder of the applicable IND. If sponsorship of the RESTORE-1 Phase 2 clinical trial is transferred back to us at our request, such transition would require additional regulatory filings with and review by the FDA, and would likely lead to additional costs and delays in the enrollment of patients in any potential future clinical trials we or a collaboration partner would pursue in connection with the VY-AADC Program.

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 (NB1b-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 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. In November 2020, the sponsor medical monitor and surgical core requested that the data safety and monitoring board, or DSMB, for the RESTORE-1 Phase 2 clinical trial review certain patient MRI abnormalities observed in some clinical trial participants in the ongoing clinical trial. Following this review, the DSMB requested additional patient-level data and recommended a pause in the dosing of patients in the RESTORE-1 Phase 2 clinical trial pending its review of these additional data. In response to the DSMB's recommendation, we and Neurocrine decided to delay the planned resumption of patient screening in the RESTORE-1 Phase 2 clinical trial until Neurocrine had submitted the required expedited IND safety reports related to these matters and the DSMB was able to complete its evaluation. In December 2020, the FDA notified Neurocrine that it had placed a clinical hold on the RESTORE-1 Phase 2 clinical trial. In January 2021, the FDA informed Neurocrine of the information required to provide a complete response to the FDA in connection with the clinical hold. Information required by the FDA includes an assessment of how the investigational product may have given rise to the adverse findings, a mitigation plan to manage the adverse findings, and supportive data to justify that the product candidate continues to have a favorable benefit/risk profile. The DSMB met to review additional patient data in January 2021 and characterized the MRI abnormalities as having uncertain clinical significance and requested that Neurocrine provide additional information. The clinical implications of these observations are currently unknown. We intend to support Neurocrine, the clinical trial sponsor and IND holder, on ongoing matters related to the completion of imaging and clinical assessments requested by the DSMB and the provision of other information requested by the FDA for the RESTORE-1 Phase 2 clinical trial. We have decided that, if Neurocrine were to transfer sponsorship of the RESTORE-1 Phase 2 clinical trial back to us, we would not seek to advance the clinical trial without a partner. Our ability to establish such a collaboration regarding the VY-AADC Program will be subject to a number of factors, including, among other things, the additional information collected by Neurocrine in response to the DSMB requests.

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 and other diseases;
- perceived risks of the delivery procedure, such as the intracranial infusions previously proposed for evaluation in connection with VY-AADC (NB1b-1817) and VY-HTT01;

- 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, particularly for clinical trials requiring lengthy and highly complex surgical protocols, the performance of which may only be possible at major academic medical centers or specialized surgical centers;
- 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, management, or other aspects of the clinical trial;
- 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, such as the clinical hold that the FDA placed on the IND application for the RESTORE-1 Phase 2 clinical trial of VY-AADC (NB1b-1817) in Parkinson's disease in December 2020;
- as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites or the decision by us or our collaborators, such as the pause in screening and enrollment of patients in the RESTORE-1 Phase 2 clinical trial in Parkinson's disease, 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;
- 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;

## [Table of Contents](#)

- 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 initiate or 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. For example, our decision to refocus our Huntington's Disease program means we must conduct new preclinical studies, prepare a new IND, submit it to the FDA, and resolve any potential FDA objections before enrolling our first patient in a new clinical trial. 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 or as a result of unanticipated clinical trial results, 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 were designed to be administered directly to the targeted areas and cells in the brain, requiring the patient to undergo brain surgery. There are risks associated with direct delivery of AAV gene therapy into the brain. 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). Investigators in the PD-1101 Phase 1b clinical trial, the separate PD-1102 Phase 1 posterior trajectory trial, and the RESTORE-1 Phase 2 clinical trial of VY-AADC (NBIB-1817), have used 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. One patient in the Phase 1b clinical 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). Limited clinical data are available for this route of administration. If other side effects were to occur in connection with this route of administration including the related surgical procedures or related devices, any clinical trials which we conduct utilizing intraparenchymal delivery could be suspended or terminated. While we intend to transition our product candidates away from direct delivery into the brain, our experience outside of direct delivery is limited, and we may not see the levels of results we hope for using alternative delivery methods such as intravenous delivery.

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. We believe that the likelihood of the FDA requiring a REMS may be higher for treatments with more invasive routes of administration such as direct delivery through brain surgery. 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 regulatory 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. 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.

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 certain of our current programs may qualify for orphan drug designation. 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. This designation, however, does not mean that we will be able to obtain orphan drug designation for any future or related product candidates for the treatment of Huntington’s disease, including our planned second-generation product candidate for 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 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 September 2021, the FDA issued final guidance describing its current thinking on when a gene therapy product is the "same" as another product for purposes of orphan exclusivity. Under the guidance, if either the transgene or vector differs between two gene therapy products in a manner that does not reflect "minor" differences, the two products would be considered different drugs for orphan drug exclusivity purposes. The FDA will determine whether two vectors from the same viral class are the same on a case-by-case basis and may consider additional key features in assessing sameness.

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, particularly in light of a decision from the U.S. Court of Appeals for the Eleventh Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the Court of Appeals concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." 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 (NB1b-1817) gene therapy treatment for Parkinson’s disease in patients with motor fluctuations that are refractory to medical management. The designation was based on data from the PD-1101 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 (NB1b-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 application user fee to obtain FDA review of a marketing application is more than \$3.1 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.

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, vectorized antibody 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., Alcyone Therapeutics, Inc., Amicus Therapeutics, Inc., Apic Bio, Inc., Applied Genetic Technologies Corporation, Asklepios BioPharmaceutical, Inc., or AskBio (acquired by Bayer), Audentes Therapeutics, Inc. (acquired by Astellas Pharma Inc.), Biogen, Inc., or Biogen, Brain Neurotherapy Bio, Inc. (merged with AskBio), Encoded Therapeutics, Inc., GenSight Biologics SA, Homology Medicines, Inc., LEXEO Therapeutics, Inc., LogicBio Therapeutics, Inc., Lysogene SA, MeiraGTx Ltd., or MeiraGTx, Neurogene, Inc., Novartis Gene Therapies, Inc. (formerly AveXis, Inc.), Passage Bio, Inc., Pfizer, Prevail Therapeutics Inc. (acquired by Eli Lilly), PTC Therapeutics, Inc., REGENXBio Inc., Sarepta Therapeutics, Inc., Sio Gene Therapies, Inc., Solid Biosciences, Inc., Spark, StrideBio, Inc., Taysha Gene Therapies, Inc. and 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 our TRACER platform preclinical programs will compete with a variety of technologies and therapies in development, including:

- Our TRACER discovery platform will potentially compete with a variety of companies developing AAV capsids, including: 4D Molecular Therapeutics, Inc., Affinia Therapeutics Inc., Apertura Gene Therapy, LLC, Capsida Biotherapeutics, Inc., Capsigen Inc., Dyno Therapeutics, Inc., Kate Therapeutics, Inc., Shape Therapeutics, Inc., and StrideBio, Inc.
- Our program for diseases linked to GBA1 mutations will potentially compete with AAV gene therapies being developed by Prevail Therapeutics Inc. (acquired by Eli Lilly & Co.), Freeline Therapeutics Holdings plc, Pfizer, Biogen, Lysogene SA, and Coave Therapeutics;
- Our 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, Eisai Co., Ltd., Janssen

Pharmaceuticals, Inc., UCB S.A., and several other companies, as well as an antisense oligonucleotide program being developed by Ionis in collaboration with Biogen;

- Our program for a monogenic form of ALS will potentially compete with BIIB067 (IONIS-SOD1Rx) being developed by Biogen, in collaboration with Ionis, and gene therapies being developed by Apic Bio, Inc. and Novartis Gene Therapies, Inc.;
- Our program for Huntington's disease will potentially compete with AMT-130, an AAV gene therapy being developed by uniQure, a gene therapy being developed by Spark, and TAK-686 being developed by Sangamo Therapeutics, Inc. in collaboration with Takeda Pharmaceutical Company Limited;
- Our program for spinal muscular atrophy, or SMA, will potentially compete with Zolgensma being marketed by Novartis Gene Therapies, Inc., Spinraza being marketed by Biogen, and Evrysdi being marketed by Roche; and
- Our program for Friedreich's ataxia will potentially compete with AAV gene therapies being developed by LEXEO Therapeutics, Inc., AAVANTIBio, Inc., PTC Therapeutics, Inc., StrideBio, Inc. in collaboration with Takeda Pharmaceutical Company Limited, Pfizer, and Novartis Gene Therapies, Inc..

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, and a transition period to December 31, 2020, was established to allow the United Kingdom and the European Union to negotiate the United Kingdom's withdrawal. Effective January 1, 2021, the United Kingdom is no longer part of the European Single Market and European Union Customs Union. A cooperation agreement was signed between the United Kingdom and the European Union in December 2020, which was applied provisionally beginning on January 1, 2021 and entered into force on May 1, 2021. The agreement addresses trade, economic arrangements, law enforcement, judicial cooperation and a governance framework including procedures for dispute resolution, among other things. As both parties continue to work on the rules for implementation, significant political and economic uncertainty remains about how the precise terms of the relationship between the parties will differ from the terms before withdrawal.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering the 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, the consequences of Brexit and the impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom remain unclear. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of European Union law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the European Union. 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 for our product candidates, which could significantly and materially harm our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including 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 revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

***Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.***

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. The FDA announced on February 2, 2022, that it would resume domestic inspections beginning on February 7, 2022. As for foreign inspections, the FDA indicated that it would continue planned inspections in countries that have received country clearance and are within the CDC's level 1 or level 2 COVID-19 travel recommendation. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

***If approved, our product candidates that are licensed and regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.***

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA, to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. In addition, the licensure of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still develop and

receive approval of a competing biologic, so long as its BLA does not rely on the reference product, sponsor's data or submit the application as a biosimilar application. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty, and any new policies or processes adopted by the FDA could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of the product candidates we develop as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing. Nonetheless, the approval of a biosimilar to our product candidates would have a material adverse impact on our business due to increased competition and pricing pressure.

### **Risks Related to Third Parties**

***To date, all of our revenue has been derived from our prior collaborations with Sanofi Genzyme and AbbVie, our ongoing collaboration with Neurocrine, the Pfizer License Agreement, and the Novartis License Agreement. If any ongoing or future collaboration or licensing 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 VY-AADC Program, Friedreich's ataxia program, or FA Program, and the 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. 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.

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.

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. Subject to the terms and conditions of the Neurocrine Collaboration Agreement, we also have the option to co-develop and co-commercialize the FA Program with Neurocrine pursuant to which we and Neurocrine would agree to enter into a cost- and profit-sharing arrangement for such program and share in its costs, profits and losses, and we would 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.

On February 2, 2021, Neurocrine notified us that it had elected to terminate the Neurocrine Collaboration Agreement solely with regards to the VY-AADC Program. This termination became effective August 2, 2021, which we refer to as the Neurocrine VY-AADC Program Termination Effective Date. The Neurocrine Collaboration Agreement remains in full force and effect for each other program thereunder. Upon the termination of the VY-AADC Program, the license granted by us to Neurocrine regarding the VY-AADC Program expired, and we regained worldwide intellectual property rights to the VY-AADC Program in accordance with the collaboration agreement, and the restrictions on us to develop, manufacture or commercialize a gene therapy product directed to the targets specified in the VY-AADC Program terminated. If Neurocrine were to terminate the remainder of the Neurocrine Collaboration Agreement, we would become responsible for all research and development expenses relating to the remaining Neurocrine Programs and would not receive any future milestone payments or royalty payments under the Neurocrine Collaboration Agreement with respect to such programs.

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.

On October 1, 2021, we entered into the Pfizer License Agreement, pursuant to which we granted Pfizer options to receive an exclusive license to TRACER capsids to develop and commercialize certain AAV gene therapy candidates comprised of a TRACER capsid and specified transgenes to help treat respective central nervous system and cardiovascular diseases. Under the terms of the Pfizer License Agreement, we received an upfront payment of \$30.0 million in October 2021 and are eligible to receive future option exercise payments of \$10.0 million upon each of up to two option exercises; specified development, regulatory, and commercialization milestone payments following each option exercise of up to an aggregate of \$115.0 million for the first licensed product to achieve such milestones; specified sales milestone payments of up to an aggregate of \$175.0 million per licensed product; and tiered, escalating royalties in the mid- to high-single digit percentages of annual net sales of each licensed product. If Pfizer decided not to exercise its options or otherwise to terminate the Pfizer License Agreement, in whole or in part, we would not receive the applicable option exercise fees or future milestone payments or royalty payments.

In March 2022, we entered into the Novartis License Agreement, pursuant to which we granted Novartis options to receive an exclusive license to TRACER capsids to develop and commercialize certain AAV gene therapy candidates comprised of a TRACER capsid and specified genetic payloads for specific genetic targets. Under the terms of the Novartis License Agreement, we are entitled to receive an upfront payment of \$54.0 million and are eligible to receive future option exercise payments of \$12.5 million upon each option exercise; fees of \$18.0 million for each of two potential expansions of the arrangement; specified development, regulatory, and commercialization milestone payments following each option exercise of up to an aggregate of \$125.0 million for the first licensed product to achieve such milestones; specified sales milestone payments of up to an aggregate of \$175.0 million per licensed product; and tiered, escalating royalties in the mid- to high-single digit percentages of annual net sales of each licensed product. If Novartis decided not to exercise its options or otherwise to terminate the Novartis License Agreement, in whole or in part, we would not receive the applicable option exercise fees or future milestone payments or royalty payments.



Our current collaborators or any future collaborator might not be successful in obtaining approvals for the product candidates arising from our collaboration or commercializing or manufacturing the resulting products. Further, such collaborator's objectives in connection with the collaboration may not be consistent with our best interests. With respect to the rights granted to a collaborator by us, the collaborator 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.

***We have 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 have used 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 PD-1101 Phase 1b clinical trial, the separate PD-1102 Phase 1 posterior trajectory trial, and the RESTORE-1 Phase 2 clinical trial for VY-AADC (NBIB-1817) have used and may continue to use the real-time, intra-operative, MRI imaging system known as the ClearPoint System. We also considered using the ClearPoint System in our planned VYTAL Phase 1/2 clinical trial before we decided to refocus the Huntington's disease program and withdraw our existing IND. 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. Investigators have used the ClearPoint System at certain sites in the RESTORE-1 Phase 2 clinical trial and may continue 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) and VY-HTT01, 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 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 have relied on, and may in the future 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 have worked with CLPT on the manufacturing and clinical supply of the device for relevant clinical trials.

***We may seek to enter into collaborations, and out-licensing transactions in the future with other third parties. If we are unable to enter into such collaborations or out-licensing transactions, or if these collaborations or out-licensing transactions 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. For example, we entered into the Pfizer License

Agreement with Pfizer in October 2021 and the Novartis License Agreement in March 2022. We believe there is significant opportunity for out-licensing transactions related to the TRACER capsids. To maximize the potential of TRACER capsids for our own programs and out-licensing transactions, we have retained to date, and expect to retain in the future, all rights associated with such TRACER capsids other than the rights specific to their use in combination with a particular licensee's transgenes. Our likely collaborators and licensees 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 or out-licensing transactions on favorable terms or at all. Our ability to generate revenues from our collaborations and out-licensing transactions will depend on our and our collaborators and licensees' abilities to successfully perform the functions assigned to each of us in these arrangements. In addition, our collaborators and licensees 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 or licensee is responsible could be harmful to the public perception and prospects of our gene therapy and vectorized antibody platforms.

Our relationship with any current or future collaborators or licensees may pose several risks, including the following:

- collaborators and licensees have significant discretion in determining the amount and timing of the efforts and resources that they will apply to these collaborations and out-licensing transactions;
- collaborators or licensees may not perform their obligations as expected or desired;
- the preclinical studies and clinical trials conducted as part of these collaborations or by our licensees may not be successful;
- collaborators or licensees 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 or licensees' strategic focus or available funding or external factors, such as an acquisition, which divert resources or create competing priorities;
- collaborators or licensees 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 or by a licensee and, consequently, may have limited ability to inform our stockholders about the status of such product candidates;
- collaborators or licensees could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators or licensees 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 or by a licensee may be viewed by our collaborators or licensees as competitive with their own product candidates or products, which may cause collaborators or licensees to cease to devote resources to the commercialization of our product candidates;
- a collaborator or licensee 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 or licensees, 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 (in the case of collaborations) or may result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators or licensees 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 or out-licensing transactions;
- collaborators or licensees may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- the terms of our collaboration or license 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 and license agreements may not lead to the development or commercialization of product candidates in the most efficient manner, or at all. If our collaborations or out-licensing transactions do not result in the successful development and commercialization of products, or if one of our collaborators or licensees terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration or out-licensing transactions. 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. In the event we are unable to achieve milestones necessary to demonstrate progress on those programs, Neurocrine may be unwilling to fund these programs at the desired levels or at all, which could require us to fund these programs to a greater extent than we have expected, to decline to pursue certain program objectives or to discontinue one or more of the programs. Additionally, subject to its contractual obligations to us, if a collaborator or licensee 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 or licensees terminates its agreement with us, we may find it more difficult to attract new collaborators or licensees, 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 and licensees.

We will face significant competition in seeking appropriate collaborators and licensees, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration or license agreement with any future collaborators and licensees will depend, among other things, upon our assessment of the collaborator or licensee's resources and expertise, the terms and conditions of the proposed collaboration or out-licensing transactions and the proposed collaborator or licensee'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 or licensee may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration or out-licensing transaction 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 or licensees. 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 and licensees.

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 or out-licensing transactions 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 and vectorized antibody platforms. 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 PD-1101 Phase 1b clinical trial of VY-AADC (NB1b-1817) and the separate PD-1102 Phase 1 clinical trial exploring the delivery of VY-AADC (NB1b-1817) using a posterior trajectory were conducted at several locations. The protocol for the RESTORE-1 Phase 2 clinical trial states that the clinical trial is intended to be conducted at over twenty clinical trial sites, including neurosurgical and neurology patient referral sites. Additionally, we had expected to initiate the planned VYTAL Phase 1/2 clinical trial for VY-HTT01 at multiple sites in the United States before our decision to refocus the Huntington's disease program and develop a second-generate program candidate. If any locations terminate a particular clinical trial, we or our collaborators would be required to find other parties or locations to conduct such clinical trial. 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**

***Our gene therapies 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 research 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 eliminates 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.

***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.

We presently manufacture our products using either an insect cell AAV production system or a mammalian cell system. We are aware of third parties which also use these systems in the manufacture of their products and who hold intellectual property on their AAV manufacturing systems. If we determine that access to certain third-party intellectual property is necessary for the manufacturing of our products and product candidates and are unable to license or otherwise access this intellectual property, 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 and vectorized antibody platforms. Research programs to identify new product candidates require substantial technical, financial and human resources. The only active clinical trial for a product candidate we have developed, the RESTORE-1 Phase 2 clinical trial, is currently on clinical hold. It is uncertain when, or if, the FDA might release the hold. Although our collaboration partner Neurocrine has terminated our collaboration regarding VY-AADC, Neurocrine remains the sponsor of the RESTORE-1 Phase 2 clinical trial. Our other product candidates are in preclinical development. Our portfolio of product candidates is subject to change as we continue to conduct preclinical testing and development of product candidates and prioritize or abandon product candidates based on such results and other factors. For example, in August 2022, we announced a re-prioritization of our portfolio based on a review evaluating our programs based on, among other things, their potential for competitive differentiation, supportive preclinical data, an efficient path to human proof of biology or proof of mechanism (reflecting the availability of validated biomarkers), unmet medical need, commercial opportunity, and alignment with our overall strategy. We may also fail to identify other 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. Several of our current preclinical programs have previously been part of collaborations with third parties. While we have invested significant resources in these programs, we may decide in the future to cease development activities on one or more of them.

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. 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.

We are recruiting individuals to serve as our Chief Financial Officer and as our Chief Scientific Officer on a full-time basis. Recruiting for these positions, and recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, is 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, the termination of relationships with collaborators, and the reduction of our workforce in connection with the development of a new portfolio and platform strategy 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 in connection with the August 2021 strategic restructuring, 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 foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could 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 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. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed the ACA into law. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These 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.

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. 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 inseparable 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. On December 18, 2019, the Court of Appeals for the Fifth Circuit 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. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On June 17, 2021, the U.S. Supreme Court dismissed this case after finding that plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Executive Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies

that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

***The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our drug products, if and when approved.***

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States and other jurisdictions. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted 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 products. To those ends, President Trump issued several Executive Orders intended to lower the costs of prescription drug products. Certain of these Executive Orders are reflected in recently promulgated regulations, including an interim final rule implementing President Trump's most favored nation model, but such final rule is currently subject to a nationwide preliminary injunction. It remains to be seen whether these Executive Orders and resulting regulations will remain in force during the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has 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, health care organizations 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.

In other countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we, or our collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our products or product candidates to other available therapies. If reimbursement of our products or product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

***We may be subject, directly or indirectly, to federal, state, and foreign healthcare laws and regulations, including fraud and abuse laws and false claims 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 research and development, 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, with potential liability including mandatory treble damages and significant per-claim penalties. 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 and other countries. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws such as laws of individual European Union Member States or 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.

***We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.***

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the United States, European Union, and United Kingdom. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

In 2018, California passed into law the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the European Union's General Data Protection Regulation, or GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. On November 3, 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or CPRA, which will significantly expand the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. Most CPRA provisions are scheduled to take effect on January 1, 2023, though the obligations will apply to any personal information collected after January 1, 2022. These provisions may apply to some of our business activities. In addition, other states, including Virginia and Colorado, already have passed state privacy laws. Congress, at the federal level, and other states are expected to consider similar laws in the future. These laws may

impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

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 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.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. Following Brexit, the Data Protection Act of 2018 applies to the processing of personal data that takes place in the United Kingdom and includes parallel obligations to those set forth by GDPR. Privacy and data security laws in several other countries loosely follow GDPR as a model but often contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and any eventual commercialization and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions. Any failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

***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.

***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. 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. Our corporate headquarters is in Massachusetts, a state particularly hard hit by the initial wave of the pandemic. We have and will continue to adhere to applicable guidelines and safety measures including guidelines and measures regarding 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. Although the entirety of our workforce has been permitted to return to the office for a portion of the work week, workplace safety measures still in effect continue to limit our workforce's ability to collaborate as it did prior to the COVID-19 pandemic. Further, the COVID-19 pandemic has transformed the workplace, establishing as an expected business norm a hybrid working environment where employees who are able to perform their job responsibilities remotely will expect the flexibility to work in locations outside of our office facilities. This type of workplace environment could create potential challenges, including establishing equity and inclusiveness among employees who must work on-site and employees who can work remotely, sustaining a collaborative team environment and encouraging company loyalty and diminishing turnover. Our ability to develop strategies and practices to address these risks are unknown.

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.

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 potential construction projects, resulting in program delays, cost increases and disruption to our current laboratory activities and general operations. Prolonged stay-at-home policies and, as described above, 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.



## **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 agreed to fund the clinical development through the readout of the RESTORE-1 Phase 2 clinical trial for VY-AADC (NBIB-1817). If Neurocrine had not terminated the Neurocrine Collaboration Agreement with respect to VY-AADC (NBIB-1817), after the data readout of the RESTORE-1 Phase 2 clinical trial, we would have had 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 has agreed to fund the development through the Phase 1 clinical trial of VY-FXN01. After the data readout of the Phase 1 clinical 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 and vectorized antibody approaches utilize 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 and vectorized antibody therapies remain novel technologies, 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. Adverse events and SAEs in our clinical trials such as the MRI abnormalities detected in some patients dosed in the RESTORE-1 Phase 2 clinical trial, 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, from natural disasters including earthquakes, typhoons, floods and fires, or from economic, social, 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 creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. 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. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

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 currently co-own certain intellectual property rights with one or more third parties. We may not be able to obtain a license to the third parties' interest such that we have exclusive access and control of such co-owned assets. In this case, and depending on the jurisdiction of the patent filing, we may not be able to license, enforce, or exploit the co-owned rights without the consent from, or an accounting to, the other co-owners.

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. We may also decide not to exercise an option to such institutional rights.

If we decide not to obtain, or 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 licensors 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 2021 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 licenses or licensors 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 licenses or licensors 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. For example, we have been made aware by a third party of certain patents claiming processes that may relate to, and could potentially be asserted against, DNA preparation processes related to our TRACER discovery platform. We are not practicing any processes claimed in these patents and, accordingly, we believe that our TRACER discovery platform does not infringe any valid claims in these patents. 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 licenses or licensors, 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. 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 method of treatment claims, 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 U.S. 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 U.S. 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.***

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars.

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 BPCIA 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.” 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. The recent departures of certain executives, key employees, consultants or advisors, and the restructuring of our organization, may make it more difficult to enforce our rights in protecting this information. Further, 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 policies 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 and vectorized antibody platforms 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 USPTO and other patent offices were, and may again in the future be, 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 direct or electronic access to these tribunals be interrupted or become non-existent again in the future, 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, Neurocrine, EcoR1 Capital, LLC, and The Vanguard Group, Inc. represent beneficial ownership, in the aggregate, of approximately 45% of our outstanding common stock as of June 30, 2022. 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.

***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 registration statements 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, 2022 through June 30, 2022, the sales price of our common stock ranged from a high of \$10.60 to a low of \$4.61 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, including in connection with our strategic restructuring;
- 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. We and certain of our current and former officers and directors were previously named as defendants in a purported class action lawsuit. This proceeding and other similar 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 a “smaller reporting company” and the reduced disclosure requirements applicable to such companies may make our common stock less attractive to investors.***

We are a “smaller reporting company,” as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended. We would cease to qualify as a smaller reporting company if we have (i) a non-affiliate public float in excess of \$250 million and annual revenues in excess of \$100 million during our last fiscal year, or (ii) a non-affiliate public float in excess of \$700 million, in each case determined on an annual basis as of the last business day of our second quarter. As a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not smaller reporting companies. These exemptions include:

- being permitted to provide only two years of audited consolidated financial statements in this Annual Report on Form 10-K, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- reduced disclosure obligations regarding executive compensation; and
- not being required to furnish a stock performance graph in our annual report.

We expect to take advantage of some or all of the available exemptions until we cease to be a smaller reporting company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

***We have recently been, and could in the future be, subject to legal actions and proceedings related to the decline in our stock price, which could distract our management and could result in substantial costs or large judgments against us.***

The market prices of securities of companies in the biotechnology and pharmaceutical industry, including the market price of our common stock, have been extremely volatile and have experienced fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. On January 22, 2021, a putative class action lawsuit was filed in the U.S. District Court for the Eastern District of New York (later transferred to the U.S. District Court for the District of Massachusetts) against us and certain of our current and former officers and directors. The complaint sought, among other things, unspecified compensatory damages, interest, attorneys’ and expert fees and costs. On July 2, 2021, the lead plaintiff voluntarily dismissed the action without prejudice against all defendants and as to all claims, and this action is no longer pending. Nonetheless, due to the volatility in, or the unfulfilled expectations of stockholders for, our stock price, we may be the target of similar litigation in the future.

In connection with such legal proceedings, we could incur substantial costs and such costs and any related settlements or judgments may not be covered by insurance. We could also suffer an adverse impact on our reputation and a diversion of management’s attention and resources, which could cause serious harm to our business, operating results and financial condition.

***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, 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 are required to furnish a report by our management on our internal control over financial reporting. To remain compliant with Section 404, we must continue to engage in the process of documenting and evaluating 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 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.

## **General Risk Factors**

***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, including inflation and supply disruption. A domestic or global financial crisis can cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, which could result from an event like the COVID-19 pandemic or the recent global sanctions imposed by countries against Russia following Russia's military intervention in the Ukraine, could result in a variety of risks to our business,

including weakened demand for our product candidates, our inability to purchase necessary supplies on acceptable terms, if at all, and our inability to raise additional capital when needed on acceptable terms, if at all. 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.

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

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes in tax law (which may have retroactive application) may adversely affect our stockholders or our business or financial condition. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. On December 22, 2017, the U.S. government enacted the TCJA, which significantly revised the Internal Revenue Code of 1986, as amended, or the Code. 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, or NOLs, to 80% of current year taxable income and elimination of NOL carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such NOLs 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. Beginning in 2022, the TCJA eliminates the currently available option to deduct research and development expenditures and requires taxpayers to amortize them over five years. Congress is considering legislation that would defer the amortization requirement to future periods, however, we have no assurance that the provision will be repealed or otherwise modified.

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, the CARES Act was enacted on March 27, 2020 and COVID-19 relief provisions were included in the Consolidated Appropriations Act, 2021 or CAA, which was enacted on December 27, 2020. All 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 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, the CARES Act and the CAA 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 possible that Congress will enact additional legislation in connection with the COVID-19 pandemic, and as a result of the changes in the U.S. presidential administration and control of the U.S. Senate, additional tax legislation may also be enacted; any such additional legislation could have an impact on us. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act, the CARES Act or the CAA.

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

As of December 31, 2021, we had both federal and state NOL carryforwards of \$210.8 million and \$198.9 million, respectively, which expire beginning in 2033. These NOL 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 NOL carryforwards that may

significantly impact our ability to utilize our NOLs 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 NOLs generated in one state cannot be used to offset income generated in another state. Furthermore, the use of NOL carryforwards may become subject to an annual limitation under Section 382 of the Code and similar state provisions in the event of certain cumulative changes in the ownership interest of significant shareholders in excess of 50 percent over a three-year period. This could limit the amount of NOL carryforwards that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of a company immediately prior to the ownership change. Our company has completed several transactions since its inception which resulted in an ownership change under Section 382 of the Code. In addition, future changes in our stock ownership, some of which are outside of our control, could result in ownership changes in the future. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

***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, ransom requests, 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 or to use such access to request cash compensation in the form of a ransom for the return of such 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, or a loss of cash in response to ransom threats, we could incur liability, our competitive and financial 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.

***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.



**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:				Filed Herewith
		Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number	
10.1	<a href="#">Consulting Agreement by and between the Registrant and Glenn Pierce, M.D., Ph.D., effective as of June 6, 2022</a>	8-K	10.1	06/07/2022	001-37625	
10.2	<a href="#">Lease Termination Agreement by and between the Registrant and BRE-BMR Pilgrim &amp; Sidney LLC, dated as of June 22, 2022</a>	8-K	10.1	06/23/2022	001-37625	
10.3	<a href="#">Sublease Termination Agreement by and between the Registrant and BioNTech US, Inc., dated as of June 22, 2022</a>	8-K	10.2	06/23/2022	001-37625	
31.1	<a href="#">Certification of Principal Executive Officer pursuant to Exchange Act Rules 13a-14 or 15d-14.</a>					X
31.2	<a href="#">Certification of Principal Financial Officer pursuant to Exchange Act Rules 13a-14 or 15d-14.</a>					X
32.1+	<a href="#">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.</a>					X
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because 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.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover Page Interactive Data File – The cover page interactive data file does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					

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

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: August 4, 2022

**VOYAGER THERAPEUTICS, INC.**

By: /s/ Alfred Sandrock, M.D., Ph.D.  
Alfred Sandrock, M.D., Ph.D.  
Chief Executive Officer, President, and Director  
(Principal Executive Officer)

By: /s/ Julie Burek  
Julie Burek  
Vice President, Finance  
(Principal Financial and Accounting Officer)

## Certification

I, Alfred Sandrock, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the period ended June 30, 2022 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 4, 2022

*/s/ Alfred Sandrock, M.D., Ph.D.*

Alfred Sandrock, M.D., Ph.D.  
Chief Executive Officer, President, and Director  
(Principal Executive Officer)

---

## Certification

I, Julie Burek, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the period ended June 30, 2022 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 4, 2022

*/s/ Julie Burek*

---

Julie Burek  
Vice President of Finance  
(Principal Financial and Accounting Officer)

---

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

In connection with the Quarterly Report on Form 10-Q of Voyager Therapeutics, Inc. (the "Company") for the period ended June 30, 2022, 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 4, 2022

*/s/ Alfred Sandrock, M.D., Ph.D.*

\_\_\_\_\_  
Alfred Sandrock, M.D., Ph.D.  
Chief Executive Officer, President, and Director  
(Principal Executive Officer)

Date: August 4, 2022

*/s/ Julie Burek*

\_\_\_\_\_  
Julie Burek  
Vice President of Finance  
(Principal Financial and Accounting Officer)

---