voyager
THERAPEUTICS

2022
ANNUAL REPORT

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TO OUR SHAREHOLDERS

Voyager has undergone a transformation since I became CEO in March of 2022. We have advanced a pipeline focused on some of the most significant unmet needs in neurology, achieved breakthrough innovations in novel capsid discovery including the identification of the receptor for one class of capsids, and entered or advanced multiple high-value collaborations. The expanded partnership with Neurocrine Biosciences that we announced in January 2023 demonstrates the value of our next-generation gene therapies for central nervous system (CNS) diseases, and the decisions of gene therapy leaders Pfizer and Novartis to exercise options to license our capsids illustrate the value of our platform. Thanks to this progress, during a time when the markets have been difficult for much of the biotechnology sector, we have created value for our shareholders, and we have made important steps towards developing transformational therapies for patients.

I believe we're witnessing a renaissance in neurotherapeutics. Just this year, the second disease-modifying therapy for Alzheimer's disease received accelerated approval, and the first drug was approved for Friedreich's ataxia. We've seen breakthroughs in treating negative symptoms of schizophrenia, something for which there are no approved therapies. The FDA recently granted accelerated approval to an antisense oligonucleotide for SOD1 amyotrophic lateral sclerosis (ALS), after the FDA advisory committee found that treatment-driven reductions in neurofilament are reasonably likely to predict clinical benefit in SOD1-ALS patients.

A key issue limiting the neurotherapeutics field today is delivery. Thanks to the revolution in human genetics and genomics, we now have a much clearer picture of the causes, in molecular terms, of many neurological diseases, which has led to well-validated drug targets—a huge difference from when I first entered this area 25 years ago. Companies such as Voyager have expanded far beyond small molecules to access those targets, with modalities including nucleic acid-based therapies like siRNA, monoclonal antibodies, and gene therapies. But the blood-brain-barrier constrains CNS delivery of these therapies, and intrathecally administered therapies often don't penetrate the deep areas of the brain implicated in many neurologic diseases.

The TRACER™ capsid discovery platform is the foundation of our approach to solving this delivery challenge. Voyager scientists have engineered multiple capsid libraries, each with more than 20 million novel variants of AAV5 and AAV9 capsids, to select those novel capsids that display greatly increased transduction in the CNS following intravenous delivery in preclinical studies. During 2022, we made significant progress leveraging our novel capsids to advance gene therapy programs for our collaboration partners as well as advancing our own pipeline.

Our wholly owned SOD1-ALS program combines a TRACER-derived capsid for CNS delivery with a potent siRNA construct designed to address the toxic gain of function in this form of ALS. We believe proof of concept for the therapeutic hypothesis has been demonstrated by the antisense oligonucleotide therapy tofersen, which recently received accelerated approval from the FDA, blazing a trail that we could follow with a gene therapy solution designed to provide longer duration of benefit, one-time dosing, and greater CNS penetration. We are continuing to conduct preclinical studies to select a development candidate.

Our wholly owned anti-tau monoclonal antibody program for Alzheimer's disease is designed to block the spread of pathological tau in patients with Alzheimer's disease. We believe our program is differentiated from other antibodies that have not demonstrated clinical efficacy by targeting the C-terminal rather than the N-terminal region. Moreover, our C-terminal antibody blocks the spread of pathological tau in animal models whereas N-terminal antibodies do not, and in our hands the mid-domain antibodies have yielded inconsistent results. In January 2023, we selected a humanized development candidate to advance into IND-enabling studies, and we presented data on the selection of this candidate at the 2023 AD/PD Conference in Sweden in March. We expect to initiate IND-enabling studies this year.

We have multiple partnered programs with attractive economics and opt-in rights for Voyager. The recent expansion of our strategic collaboration with Neurocrine Biosciences provided $175 million upfront and up to $4.2 billion in potential milestones for rights to our GBA1 gene therapy program for Parkinson's disease and three additional gene therapy programs directed to rare CNS targets. We are also collaborating with Neurocrine to advance our FXN gene therapy for Friedreich's ataxia towards IND submission. Neurocrine has agreed to fully fund both the GBA1 and FXN programs through Phase 1, at which point Voyager has options to co-develop and co-commercialize the assets in the U.S. We announced in March 2023 that Novartis exercised its option to license TRACER capsids against two neurologic disease targets, triggering a $25 million option exercise fee and making Voyager eligible to receive up to $600 million in milestone payments. This followed Pfizer's decision in October 2022 to exercise its option to license a capsid against a CNS target.

Our track record of generating non-dilutive funding from collaborations has substantially bolstered our balance sheet, enabled the advancement of our wholly owned pipeline, and created potential strategic upside through deal structures such as co-development/co-commercialization options. With our strong progress in 2022, we announced we are building a sustainable pipeline of genetic medicines for neurological diseases, introducing two new early research initiatives: an allele-specific mHTT + MSH3 combination gene therapy for Huntington's disease and a tau knockdown gene therapy for Alzheimer's disease.

Voyager has made significant strides over the past year in the advancement of our programs and platform, which has translated into validating partnerships and increased value to our shareholders. I'm more excited than ever for the future, and it is a privilege to lead our outstanding team at Voyager as we advance neuro-genetic medicines for diseases of great unmet need. Our team is an inspiration to me as we work every day to advance these therapies to help patients.

Sincerely,

Alfred Sandrock, M.D., Ph.D.
President and Chief Executive Officer

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____

Commission File Number: 001-37625

Voyager Therapeutics, Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**46-3003182**
(State or Other Jurisdiction of Incorporation or Organization)	**(IRS Employer Identification No.)**
64 Sidney Street, Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

(857) 259-5340
(Registrant's Telephone Number, Including Area Code)

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 if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. **Yes** ☐ **No** ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. **Yes** ☐ **No** ☒

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

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

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

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

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

The aggregate market value of Common Stock held by non-affiliates of the registrant computed by reference to the price of the registrant's Common Stock as of June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $113.6 million (based on the last reported sale price on the Nasdaq Global Select Market as of such date).

As of March 1, 2023, there were 43,293,369 shares of the registrant's common stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2023 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Proxy Statement is expected to be filed with the U.S. Securities and Exchange Commission not later than 120 days after the end of the fiscal year to which this report relates.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, 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 and our vectorized antibody platform, and our proprietary antibodies;
- our ability to identify and optimize product candidates and proprietary AAV capsids;
- our strategic collaborations with and funding from our collaboration partner Neurocrine Biosciences, Inc., or Neurocrine, from our option and license arrangement with Pfizer Inc., or Pfizer, and from our option and license arrangement with Novartis Pharma AG, or Novartis;
- our ongoing and planned preclinical development efforts, related timelines and studies;
- our ability to enter into future collaborations, strategic alliances, or option and license arrangements;
- 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, contingent liabilities, future revenues, existing cash resources and capital requirements;
- 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;
- our need for additional funding and our plans and ability to raise additional capital, including through equity offerings, debt financings, collaborations, strategic alliances, and option and license 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; and
- our ability to control costs and prioritize our product candidate pipeline successfully in connection with our strategic initiatives.

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 Annual Report on Form 10-K, 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, strategic collaborations, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to the Annual Report on Form 10-K 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 I, Item 1A - Risk Factors" and elsewhere in this Annual Report on Form 10-K. 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.

- Our AAV gene therapy and other biological therapy 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. All of our active product candidates are currently in preclinical 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.

- 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.

- To date, all of our revenue has been derived from our ongoing collaborations with Neurocrine, from our ongoing option and license arrangements with Pfizer and Novartis, and from our prior collaborations with Sanofi Genzyme Corporation, AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company. If any ongoing or future collaboration or option and license agreements were to be terminated, our business financial condition, results of operations and prospects could be harmed.

- 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 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 gene therapy and vectorized antibody approaches utilize vectors derived from viruses that are selectively engineered, 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.

PART I

ITEM 1. BUSINESS

We are a biotechnology company dedicated to breaking through barriers in gene therapy and neurology. We believe the potential of both disciplines has been constrained by delivery challenges; we are leveraging expertise in capsid discovery and neuropharmacology to address these constraints. 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 other biological therapy 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 an AAV vector or other biological therapy for activity in, efficacy in, or delivery to, the targeted tissue or cells.

We are identifying proprietary AAV capsids, the outer viral protein shells that enclose genetic material that makes up the vector payload. Our team has developed a proprietary AAV capsid discovery platform called TRACER™ (Tropism Redirection of AAV by Cell Type-Specific Expression of RNA) that employs directed evolution to facilitate the selection of AAV capsids with enhanced tissue delivery characteristics, such as more effective delivery across the blood brain barrier, or BBB. 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 that capsids we discover through our TRACER discovery platform, which we refer to as TRACER capsids, have the potential to significantly enhance the efficacy and safety of our single dose gene therapies, which we expect to be delivered with systemic infusions, as compared with conventional capsids.

In addition to leveraging TRACER capsids in potential licensing arrangements, we are advancing our own proprietary pipeline of drug candidates for neurological diseases. Our wholly-owned prioritized pipeline programs include: superoxide dismutase 1, or SOD1, gene therapy for amyotrophic lateral sclerosis, or ALS, and an anti-tau antibody for Alzheimer's disease. We have identified a lead development candidate for our anti-tau antibody program and we expect to identify a lead development candidate for our SOD1 program during the first half of 2023. We expect to file INDs for both programs in 2024. In addition to these two wholly-owned programs, we are actively advancing two programs in collaboration with Neurocrine: a glucocerebrosidase 1, or GBA1, gene therapy program for Parkinson's disease and other GBA1-mediated diseases, and a FXN gene therapy program for Friedreich's ataxia. We also maintain a robust early research pipeline of wholly-owned and collaborative gene therapy programs for neurological diseases.

Mission and Strategy

Our mission is to is leverage our expertise in neuroscience and our pioneering discoveries in AAV capsids to advance life-changing gene therapies and other therapeutic modalities for neurological diseases. Our strategy to achieve this mission is to:

- ***Continuously advance in the development of our AAV gene therapy platform***. We plan to continuously invest in our gene therapy platform to maintain our strong position in the development of next-generation AAV gene therapies for neurological disorders and other serious diseases.

- ***Optimize and advance our gene therapy programs***. We have a pipeline comprised of a variety of preclinical programs that we intend to enable with proprietary, next-generation AAV capsids.

- ***Partner and collaborate to maximize the opportunities for our pipeline of gene therapy programs focused on severe neurological diseases and other serious diseases***. We believe that our experience in AAV gene therapy for severe neurological diseases, our pipeline of gene therapies, and our gene therapy platform provide us with the opportunity to collaborate to enhance our portfolio's long-term value.

- ***Partner with gene therapy developers to make available AAV capsids identified by our TRACER system***. We expect to make these capsids available through potential licensing agreements and other arrangements.

- ***Establish a leadership position in high quality AAV manufacturing***. We believe that manufacturing capacity and expertise are critical to successfully treating patients using gene therapy.

- ***Retain commercialization rights to select pipeline programs.*** We hold worldwide rights to our proprietary pipeline programs for various diseases and have retained certain commercialization rights for other programs.

- ***Expand our intellectual property portfolio***. We seek to have an industry-leading intellectual property portfolio across all facets of our business, including vector engineering and construct design, proprietary capsids, our production process, the compositions and methods of delivery of our product candidates.

AAV Gene Therapy

Gene therapy is an approach whereby gene expression is directly altered in patients to address the underlying cause or predominant manifestations of disease. We believe that the targeted nature of gene therapy may enable powerful treatment options and provide these patients with meaningful and durable benefits.

While AAV gene therapy can potentially be harnessed for multiple treatment methods, we are currently focused on gene replacement, gene knockdown and vectorized antibody approaches. Gene replacement is intended to restore the expression of a protein that is not expressed, expressed at abnormally low levels or functionally mutated with loss of function. Gene knockdown, or gene silencing, is intended to reduce the expression of a pathologically mutated RNA or protein that has detrimental effects. Vectorizing an antibody for delivery using AAV has the ability to increase exposure of large antibodies in brain parenchyma and interstitial fluid that otherwise show minimal penetration across the BBB when administered passively. Our gene therapy approach uses AAV vectors which we believe are ideal vectors for gene therapy for several reasons:

- ***Broad Applicability.*** AAV is able to transduce, or transfer a therapeutic gene, into numerous cell types including target cells in the central nervous system, or CNS, cardiac, and other tissues.

- ***Safety.*** We believe AAV is safe and is not known to cause any disease in humans.

- ***Does Not Readily Integrate.*** AAV does not readily integrate into the genome of the target cell, an attribute which we believe reduces the potential for oncogenesis, or the induction of cancer.

- ***Scalability.*** AAV is able to be manufactured at commercial quality and scale.

We believe that neurological diseases are well-suited for treatment with AAV gene therapy for the following reasons:

- ***Validated Targets.*** Many neurological, cardiac, and other diseases are caused by well-defined mutations in genes and these genes represent genetically validated drug targets for AAV gene therapy.

- ***Targeted Delivery.*** We believe our TRACER capsids may allow for significantly enhanced gene therapy delivery to specific types of cells and tissues at lower doses.

- ***Durable Expression.*** Long-term gene expression may be achievable in the CNS and other tissues following one-time dosing and transfer of the therapeutic gene with an AAV vector. Because repeated or continual dosing with direct injection of drugs into the CNS and other tissues is complex, a one-time AAV gene therapy has significant advantages.

The Voyager Gene Therapy Platform

We have built a gene therapy platform that we believe positions us to be the leading company at the intersection of AAV gene therapy and neurological diseases. Our team of experts in the field of AAV gene therapy first identifies and selects diseases that are well-suited for treatment using AAV gene therapy. We then engineer and optimize AAV vectors, identifying a capsid for delivery of a payload, comprising a therapeutic gene or transgene, and a promoter to drive expression of the transgene, to the targeted tissue or cells. Finally, we leverage established routes of administration and advances in dosing techniques to optimize delivery of our AAV vectors to target cells that are critical to the disease of interest. We believe that optimizing each of these parameters is a key factor for overall program success. We expect that our current and future pipeline programs will make use of technological advances generated with our gene therapy platform.

Disease Selection

Following an internal review process, we have prioritized pipeline programs for our development. This review evaluated the opportunity presented by each prioritized program based on the following criteria: high unmet medical need, target validation, efficient path to human proof of biology, robust preclinical pharmacology, and strong commercial potential.

Vector Engineering and Optimization

The key components of an AAV vector include: (a) the capsid; (b) the therapeutic gene, or transgene; and (c) payload control elements, including the promoter or other DNA sequences that modulate the expression of the transgene. 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. We have also built, or intend to build, capabilities to design, screen, and advance genetic sequences within our AAV vectors, including transgenes and payload control elements, to create optimized therapeutic candidates for each of our preclinical programs.

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. 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 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.

We are actively engaged in discussions to make TRACER capsids available to third parties for use in their drug development programs through potential option and license and other arrangements. We believe there is significant opportunity for option and license transactions related to our TRACER capsids. To maximize the potential of our TRACER capsids for both our own programs and option and license 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 optionee's or licensee's transgenes or collaborators' programs.

Collaboration Agreements

In January 2019, we entered into a collaboration with Neurocrine, or the 2019 Neurocrine Collaboration Agreement, for the research, development and commercialization of certain of our AAV gene therapy products. Under the 2019 Neurocrine Collaboration Agreement, we agreed to collaborate on the conduct of four collaboration programs, which we refer to collectively as the 2019 Neurocrine Programs: the NBIb-1817 (VY-AADC) program, or the VY-

AADC Program for the treatment of Parkinson's disease, the program for the treatment of Friedreich's ataxia, or the FA Program, including the development of the VY-FXN01 product candidate, which together with the VY-AADC Program, we refer to as the Legacy Programs, and other undisclosed programs, or the 2019 Discovery Programs and, collectively with the Legacy Programs, the 2019 Neurocrine Programs. In August 2021, the collaboration was terminated with respect to the VY-AADC Program. Under the FA Program, we and Neurocrine are currently developing a gene therapy for the treatment of Friedreich's ataxia, a debilitating neurodegenerative disease resulting in poor coordination of legs and arms, progressive loss of the ability to walk, generalized weakness, loss of sensation, scoliosis, diabetes and cardiomyopathy as well as impaired vision, hearing, and speech. Development of the two targets approved by the joint steering committee under the 2019 Discovery Program will continue into 2023.

On January 8, 2023, we entered into a collaboration and license agreement with Neurocrine, or the 2023 Neurocrine Collaboration Agreement, for the research, development, manufacture and commercialization of gene therapy products directed to the gene that encodes GBA1 for the treatment of Parkinson's disease and other diseases associated with GBA1, or the GBA1 Program, and three new programs focused on the research, development, manufacture and commercialization of gene therapies designed to address CNS diseases or conditions associated with rare genetic targets, or the 2023 Discovery Programs and, collectively with the GBA1 Program, the 2023 Neurocrine Programs. The 2023 Neurocrine Collaboration Agreement became effective on February 21, 2023. For more information, refer to Note 15 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

License Agreements

In October 2021, we entered into an option and license agreement with Pfizer, or the Pfizer Agreement, pursuant to which we 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, or Pfizer Transgenes.

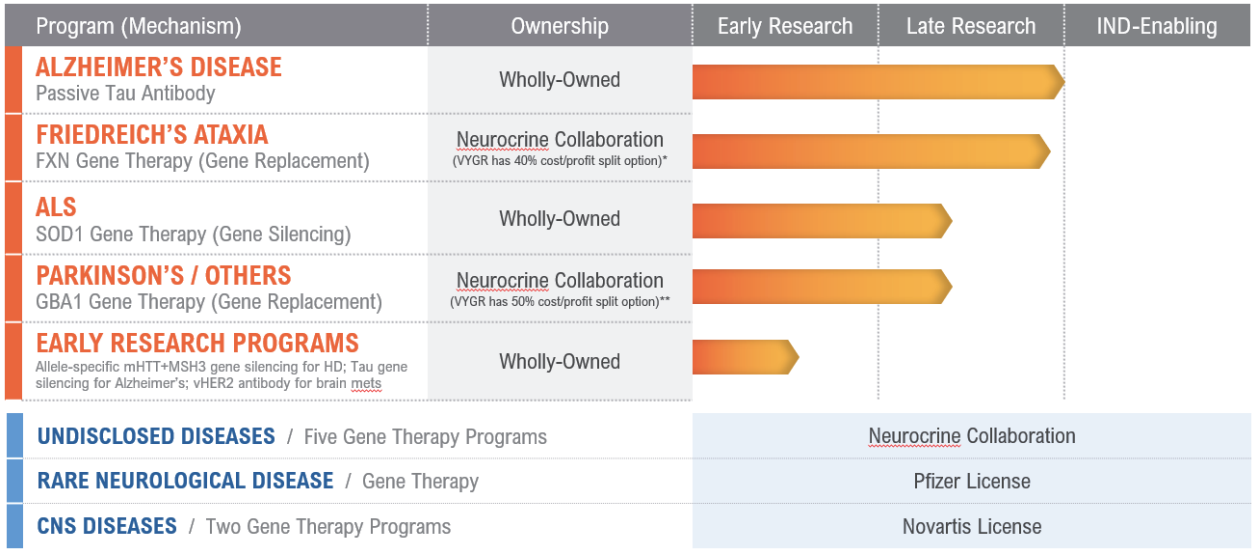
In March 2022, we entered into an option and license agreement, or the Novartis Agreement, with our collaborative partner Novartis. Pursuant to the Novartis Agreement, we have granted Novartis options, or the Novartis License Options, to license TRACER capsids, or the Novartis Licensed Capsids, for exclusive use with certain targets to develop and commercialize certain adeno-associated virus gene therapy candidates comprised of a Novartis Licensed Capsid and a payload directed to such target, or a Novartis Payload.

In November 2022, we and Touchlight IP Limited, or Touchlight, entered into a license agreement, or the Touchlight License Agreement, to authorize historical use by us of a certain DNA preparation process, or the Subject DNA Preparation Process, and to authorize the prospective exploitation of TRACER capsids created with the use of the Subject DNA Preparation Process.

Overview of Our Pipeline

We have leveraged our TRACER discovery platform and other gene therapy platforms, our expertise with proprietary antibodies, and our vectorized antibody platform to assemble a pipeline of proprietary AAV gene therapies and passive and vectorized payloads for the treatment of neurological and other diseases which we believe have high unmet medical need. Depending on the disease, we are seeking to develop AAV gene therapies that will use a gene replacement or gene silencing approach, and antibodies that will use a passive administration or vectorized delivery approach. Our goal is to address the underlying cause or the predominant manifestations of specific diseases by significantly increasing or decreasing expression of the relevant proteins in targeted tissues.

Our pipeline of our programs, all of which are in preclinical development, is summarized in the table below:



*After the Phase 1 readout, Voyager has the option to either: (1) co-develop and co-commercialize with Neurocrine Biosciences in the United States under a 60/40 cost- and profit-sharing arrangement (Neurocrine/Voyager), or (2) grant Neurocrine Biosciences full United States commercial rights in exchange for milestone payments and royalties based on United States sales.
** After the Phase 1 readout, Voyager has the option to either: (1) co-develop and co-commercialize with Neurocrine Biosciences in the United States under a 50/50 cost- and profit-sharing arrangement, or (2) grant Neurocrine Biosciences full United States commercial rights in exchange for milestone payments and royalties based on United States sales.

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

Disease Overview

We are developing proprietary antibodies that selectively target and reduce the spread of pathological tau for the treatment of tauopathies, and our lead indication is Alzheimer's disease, or AD. The spread of tau pathology closely correlates with disease progression and cognitive decline in AD, which affects approximately 6 million people in the United States, and is a growing health care burden to society. Recently, anti-amyloid antibodies have been approved for treatment of AD, and there is substantial remaining unmet medical need.

Our Treatment Approach

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 AD and other tauopathies. Reduction of toxic tau aggregates may slow disease progression and cognitive decline in these diseases. We are exploring passive administration of our anti-tau antibody. Our 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 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.

Preclinical Studies

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.

Program Status

In January 2023, we selected a lead humanized anti-tau antibody candidate to advance against AD. The lead candidate, VY-TAU01, targets the C-terminal domain. VY-TAU01 was selected for its affinity, selectivity, and biophysical characteristics. Process development and manufacturing at a contracted manufacturer have been initiated, and we expect to initiate a good laboratory practices, or GLP, toxicology study later in 2023 to enable an IND filing in the first half of 2024.

Friedreich's Ataxia Program: VY-FXN01 (2019 Neurocrine Collaboration)

Disease Overview

Friedreich's ataxia is a debilitating neurodegenerative disease resulting in poor coordination of legs and arms, progressive loss of the ability to walk, generalized weakness, loss of sensation, scoliosis, diabetes and cardiomyopathy as well as impaired vision, hearing and speech. The typical age of onset is 10 to 12 years, and life expectancy is severely reduced with patients generally dying of neurological and cardiac complications between the ages of 35 and 45. According to the Friedreich's ataxia Research Alliance, there are approximately 6,400 patients living with the disease in the United States. While one treatment for Friedreich's ataxia has recently been approved by the FDA, there remains a significant unmet need.

Friedreich's ataxia patients have mutations of the FXN gene that reduce production of the frataxin protein, resulting in the degeneration of sensory pathways and a variety of debilitating symptoms. Friedreich's ataxia is an autosomal recessive disorder, meaning that a person must obtain a defective copy of the FXN gene from both parents in order to develop the condition. One healthy copy of the FXN gene, or 50% of normal frataxin protein levels, is sufficient to prevent the disease phenotype. We therefore believe that restoring FXN protein levels to at least 50% of normal levels by AAV gene therapy might lead to a successful therapy.

Our Treatment Approach

We are seeking to develop an AAV gene therapy approach that we believe will deliver a functional version of the FXN gene to the sensory pathways through intravenous injection. We think this approach has the potential to improve balance, ability to walk, sensory capability, coordination, strength and functional capacity of Friedreich's ataxia patients. Most Friedreich's ataxia patients produce low levels of the frataxin protein, which although insufficient to prevent the disease, exposes the patient's immune system to frataxin. This reduces the likelihood that the FXN protein expressed by AAV gene therapy will trigger a harmful immune response.

Preclinical Studies

We initially conducted preclinical studies in non-human primates and achieved high FXN expression levels within the target sensory ganglia, or clusters of neurons, along the spinal region following intrathecal injection. More recently, we conducted preclinical studies in non-human primates with IV injection and achieved target FXN expression levels within sensory ganglia and the heart. The levels of FXN expression observed in the brain using an AAV vector were, on average, greater than FXN levels present in control normal human brain tissue. FXN expression was also observed in the cerebellar dentate nucleus, another area of the CNS that is often affected in Friedreich's ataxia, and that is often considered difficult to target therapeutically.

Our Program Status

As part of the 2019 Neurocrine Collaboration, we are developing VY-FXN01 for the treatment of Friedreich's ataxia. VY-FXN01 is currently in preclinical development. We and Neurocrine are in the process of identifying a lead candidate that will comprise a capsid, promoter, and FXN transgene and are evaluating the potential use of TRACER

capsids in the program. We are completing AAV capsid biodistribution experiments to confirm capsid serotypes that effectively transduce disease target tissues in non-human primates following intravenous injection. Criteria for evaluating these capsids include safety, the overall level of transgene expression achieved, and the anatomic and cellular distribution of the transgene expression. Also, we have optimized the promoter for VY-FXN01 to achieve an acceptable therapeutic index for frataxin replacement. To evaluate the therapeutic potential of our vectors, we have conducted testing in a new genetic mouse model of Friedreich's ataxia. In this preclinical model of Friedreich's ataxia, our gene therapy candidates durably improved sensory function and rescued the disease phenotype based on multiple functional tests. In physiological and behavioral assays, our gene therapy candidates demonstrated dose-dependent and durable responses for more than 10 months after a single administration, preventing central and peripheral disease progression. We also have a significant effort focused on better understanding the clinical course of Friedreich's ataxia, identifying potential fluid biomarkers and selecting clinical endpoints for future clinical trials. As part of our portfolio reevaluation and strategic shift to invest in novel capsid development efforts, we and Neurocrine are evaluating the potential use of our TRACER capsids to allow for enhanced transduction across the disease target tissues. If we and Neurocrine successfully identify a development candidate and capsid for this program, we plan to complete IND enabling studies to evaluate its safety and efficacy.

SOD1 Gene Silencing Program for the Treatment of ALS

Disease Overview

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.

Our Treatment Approach

We believe that a therapeutic delivering a vectorized highly potent small interfering RNA, or siRNA, construct via intravenous administration of an AAV gene therapy with a vectorized siRNA 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.

Preclinical Studies

At the ASGCT 2022 Meeting, 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 an SOD1-ALS mouse model following intravenous delivery of a vectorized siRNA using a mouse BBB-penetrant capsid.

Program Status

We have identified a potent and specific vectorized siRNA transgene that resulted in substantially extended lifespan and motor function when delivered using a BBB-penetrant capsid in an animal model. We are currently in the process of selecting a TRACER capsid with BBB-penetration activity in NHP studies for selection of a lead candidate vector.

GBA1 Gene Replacement Program for the Treatment of Parkinson's Disease (2023 Neurocrine Collaboration)

Disease Overview

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 glucocerebrosidase enzyme, 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 10.0 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 can decrease the activity of Gcase, leading to the accumulation of Gcase substrates which is linked to alpha-synuclein aggregates, that are thought to be toxic to neurons.

Our Treatment Approach

We believe that restoring Gcase activity may attenuate disease progression and potentially slow neurodegeneration. We anticipate delivering GBA1 via intravenous administration of an AAV gene therapy 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 be normalized 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.

Preclinical Studies

At the American Society of Gene & Cell Therapy 25th Annual Meeting in May 2022, or the ASGCT 2022 Meeting, we presented preclinical data demonstrating CNS target engagement and delivery of therapeutically relevant levels of Gcase in a GBA1 loss of function mouse model, as well as sustained expression for three or more months following intravenous administration.

Program Status

Under the 2023 Neurocrine Collaboration Agreement, we are developing gene therapy products directed to the gene that encodes GBA1 for the treatment of Parkinson's disease and other diseases associated with GBA1. The GBA1 Program is currently in preclinical development. We and Neurocrine are in the process of identifying a lead candidate that will comprise a TRACER capsid, promoter, and transgene. For more information, refer to Note 15 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Early Research Programs

In January 2023, we announced the launch of an updated early research initiative for the treatment of Huntington's disease. The updated gene therapy program, which leverages the latest insights in disease biology, combines an intravenous TRACER capsid with vectorized siRNAs to enable specific knockdown of mHTT and MSH3.

During the first quarter of 2023, we announced an early research initiative investigating a gene therapy targeting intracellular tau for the treatment of Alzheimer's disease. The program combines an siRNA tau knockdown payload with an intravenously delivered TRACER capsid.

Our wholly-owned early research programs also include a program exploring a vectorized antibody against HER2 for the treatment of brain metastases from metastatic breast cancer. Pre-clinical data has demonstrated that our vectorized antibody against HER2 is shown to inhibit proliferation and promote antibody-dependent cell cytotoxicity, a process that recruits natural killer cells, macrophages and/or brain-resident innate immune cells called microglia to eliminate tumor cells.

Collaborations and License Agreements

Pfizer Option and License Agreement

On October 1, 2021, or the Pfizer Effective Date, we entered into the Pfizer Agreement with Pfizer pursuant to which we granted Pfizer 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. Under the terms of the Pfizer Agreement, during an initial research term that ended as of October 1, 2022, or the Pfizer Research Term, Pfizer had the right to evaluate the potential use of the capsids in combination with up to two Pfizer Transgenes to help treat respective CNS and cardiovascular diseases.

Research and License Option

During the Pfizer Research Term, we agreed to provide Pfizer with certain quantities of materials encoding specified existing capsids for Pfizer's evaluation. Further, during the Pfizer Research Term, we agreed to disclose to Pfizer, on a rolling basis, the performance characteristics identified during the Pfizer Research Term for all such capsid candidates. Pfizer had 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 had the right to exercise up to two Pfizer License Options, provided that it could exercise only one Pfizer License Option for each Pfizer Transgene.

Effective as of September 30, 2022, Pfizer exercised a Pfizer License Option with respect to a capsid for the specified Pfizer Transgene for potential treatment of a rare neurological disease. Pfizer did not exercise its option to license a capsid for the potential treatment of a cardiovascular disease. As result, Pfizer's right to exercise a Pfizer License Option for a cardiovascular disease has terminated in accordance with the terms of the Pfizer Agreement and all rights to capsids for that cardiovascular disease have reverted to us. Pfizer's exercise of a Pfizer License Option extends the Pfizer Research Term to October 1, 2024, during which period 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 the rare neurological disease associated with the exercise of the applicable Pfizer License Option.

In connection with the exercise of the Pfizer License Option for a rare neurological disease, we granted Pfizer an exclusive, worldwide license, with the right to sublicense, under certain of our intellectual property, the rights to develop and commercialize rare neurological disease products utilizing the capsid candidate and incorporating the corresponding Pfizer Transgene, or the Pfizer Licensed CNS Products. Until October 1, 2024, while we are not obligated to conduct additional research activities to identify additional proprietary capsids that may be useful for AAV gene therapies for the treatment of rare neurological diseases, we have agreed to continue to disclose to Pfizer, on a rolling basis, the performance characteristics identified for all such capsid candidates that we identify during the Pfizer Research Term, if and when available. Pfizer may, during the Pfizer Research Term, conduct additional evaluations 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.

Development, Regulatory Approval and Commercialization

Under the Pfizer Agreement, Pfizer is solely responsible for, and has sole decision-making authority with respect to, development and commercialization of the Pfizer Licensed CNS Products. Pfizer is required to use commercially reasonable efforts to develop and obtain regulatory approval for at least one Pfizer Licensed CNS Product for which Pfizer has exercised its Pfizer License Option in (a) the United States and (b) at least one of the following countries: the United Kingdom, France, Germany, Italy, Spain and Japan, each of which is referred to as a Pfizer Major Market Country, subject to certain limitations. Pfizer is also required to use commercially reasonable efforts to commercialize each Pfizer Licensed CNS 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 CNS Product, subject to certain limitations.

Intellectual Property

Under the terms of the Pfizer Agreement, each of us 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 Agreement, or invented, developed, created, generated or acquired solely by or on behalf of such party after such effective date.

Exclusivity

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 Agreement and in the course of our and Pfizer's activities under the Pfizer Agreement will follow inventorship under U.S. patent law. Subject to certain limitations and exceptions, we have agreed (a) during the Pfizer 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 our 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 (b) after Pfizer's exercise of a Pfizer License Option, not to grant any third party or affiliate any right or license under our patents to exploit any licensed capsid in combination with any Pfizer Transgene.

Financial

Under the terms of the Pfizer Agreement, Pfizer has paid us an upfront payment of $30 million and a payment of $10 million in connection with the exercise of the Pfizer License Option for a rare neurological disease. We are also eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of $115 million for the first corresponding Pfizer Licensed CNS Product to achieve the corresponding milestone. On a Pfizer Licensed CNS Product-by-Pfizer Licensed CNS Product basis, we are also eligible to receive (a) specified sales milestone payments of up to an aggregate of $175 million per Pfizer Licensed CNS Product and (b) tiered, escalating royalties in the mid- to high-single-digit percentages of annual net sales of each Pfizer Licensed CNS 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.

Termination

Unless earlier terminated, the Pfizer Agreement expires on the expiration of the last-to-expire royalty term with respect to all Pfizer Licensed CNS Products in all countries. Subject to a cure period, either party may terminate the Pfizer 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 Agreement, in whole or in part, subject to specified conditions, for our insolvency, the occurrence of a violation of global trade control laws, or for our non-compliance with certain anti-bribery or anti-corruption covenants. Pfizer may also terminate the Pfizer 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 license granted by us to Pfizer under the Pfizer Agreement shall become irrevocable and perpetual, and all milestone payments and royalties that would have otherwise been payable by Pfizer under such license had the Pfizer Agreement remained in effect would be substantially reduced.

Novartis Option and License Agreement

On March 4, 2022, or the Novartis Effective Date, we entered into the Novartis Agreement with our collaborative partner Novartis. Pursuant to the Novartis Agreement, we have granted Novartis the Novartis License Options to license Novartis Licensed Capsids, for exclusive use with certain targets to develop and commercialize a Novartis Payload.

Research and License Option

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, 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, or the Initial Novartis Targets. We refer to this period, on a target-by-target basis, as the Novartis Research Term. Upon the payment of additional fees, Novartis may also assess our TRACER capsids for use with up to two other targets, or the Additional Novartis Targets, subject to certain conditions including that such target is not part of, or reasonably competitive with, our current development programs. During the Novartis Research Term, as applicable, 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 applicable Novartis Research Terms, 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 applicable 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 the Novartis Licensed Capsid.

Effective as of March 1, 2023, Novartis exercised its Novartis License Options to license novel capsids generated from our TRACER capsid discovery platform for use in gene therapy programs against two undisclosed Initial Novartis Targets. With Novartis' option exercise on two Initial Novartis Targets, we are entitled to receive a $25.0 million option exercise payment during the first half of 2023, and we are eligible to receive associated potential development, regulatory, and commercial milestone payments, as well as mid- to high-single-digit tiered royalties based on net sales of the Novartis Licensed Products incorporating the Novartis Licensed Capsids. The two Initial Novartis Targets licensed are distinct from targets in our internal and partnered pipeline. In addition, over the next 18 months, Novartis retains the right to expand the agreement to include options to license capsids for up to two Additional Novartis Targets, subject to their availability, for a fee of $18.0 million per Additional Novartis Target. Under such an expansion, we would be eligible to receive a $12.5 million license option exercise fee for each Additional Novartis Target exercised, as well as future potential milestone payments per Additional Novartis Target and mid- to high-single-digit tiered royalties on the Novartis Licensed Products incorporating the Novartis Licensed Capsids.

Novartis elected not to license a capsid for one Initial Novartis Target under the Novartis Agreement prior to the expiration of the applicable Novartis License Option. As a result, the non-exclusive research license that we granted to Novartis in connection with this Initial Novartis Target has terminated, the Novartis Research Term for this Initial Novartis Target has expired, and we are no longer eligible to receive development, regulatory, and commercial milestone payments or royalties in connection with this Initial Novartis Target. All capsid rights with respect to that Initial Novartis Target have returned to us.

Governance

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

Development, Regulatory Approval and Commercialization

Under the Novartis 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 (a) the United States and (b) 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 applicable Novartis Research Term, we have agreed to provide plasmids to Novartis for the production of TRACER capsids for evaluation upon request. We have 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 our intellectual property described above, on a Novartis Licensed Capsid-by-Novartis Licensed Capsid basis, under certain of our know-how to exploit the applicable Novartis Licensed Capsid as incorporated into Novartis Licensed Products containing the corresponding Novartis Payload.

Financial

Under the terms of the Novartis Agreement, Novartis has paid us an upfront payment of $54.0 million. Effective as of March 1, 2023, Novartis exercised its Novartis License Options to license two novel capsids generated from our TRACER capsid discovery platform for use in gene therapy programs against two undisclosed Initial Novartis Targets. With the exercise of two Novartis License Options, we have become entitled to receive a $25.0 million option exercise payment during the first half of 2023, and we are eligible to receive associated potential development, regulatory, and commercial milestone payments, as well as mid- to high-single-digit tiered royalties based on net sales of the Novartis Licensed Products incorporating the Novartis Licensed Capsids. The two Initial Novartis Targets licensed are distinct from targets in our internal and partnered pipeline. In addition, over the next 18 months, Novartis retains the right to expand the collaboration to include options to license capsids for up to two Additional Novartis Targets, subject to their availability, for a fee of $18.0 million per Additional Novartis Target. Under such an expansion, we would be eligible to receive a $12.5 million license option exercise fee for each Additional Novartis Target exercised, as well as future potential milestone payments per Additional Novartis Target and mid- to high-single-digit tiered royalties on the Novartis Licensed Products incorporating the Novartis Licensed Capsids. 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.

Intellectual Property

Under the terms of the Novartis 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 Agreement and in the course of the parties' activities under the Novartis Agreement will follow inventorship under U.S. patent law.

Exclusivity

Subject to certain limitations and exceptions, we have agreed (a) during the Novartis Research Term, as applicable, not to conduct any internal program or program on behalf of a third party that is directed to the development or commercialization of any our capsids, or grant any third party or affiliate any right or license under our 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 Targets; and (b) after Novartis's exercise of any Novartis License Option, not to grant

any third party or affiliate any right or license under our patents to exploit any Novartis Licensed Capsid for the applicable Target.

Termination

Unless earlier terminated, the Novartis Agreement expires on the expiration of the last-to-expire royalty term with respect to all Novartis Licensed Products in all countries. Subject to a cure period, either party may terminate the Novartis 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 Agreement, in whole or in part, subject to specified conditions, for our insolvency, the occurrence of a violation of global trade control laws, or for our non-compliance with certain anti-bribery or anti-corruption covenants. Novartis may terminate the Novartis Agreement, in whole or in part, for any or no reason upon ninety days' written notice to us.

Upon certain terminations for cause by Novartis, the licenses granted by us to Novartis under the Novartis 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 Agreement remained in effect would be substantially reduced.

Neurocrine Collaborations

2019 Neurocrine Collaboration Agreement

In January 2019, we entered into the 2019 Neurocrine Collaboration Agreement for the research, development and commercialization of certain of our AAV gene therapy products. Under the 2019 Neurocrine Collaboration Agreement, we agreed to collaborate on the conduct of the four 2019 Neurocrine Programs.

Collaboration and Licenses

Under the terms of the 2019 Neurocrine Collaboration Agreement, subject to the rights retained by us thereunder, we 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 2019 Collaboration Products, under (a) the VY-AADC Program, on a worldwide basis; (b) the FA Program, in the United States and, all countries in the world in which the 2019 Neurocrine Collaboration Agreement remains in effect with respect to the FA Program; and (c) each 2019 Discovery Program, on a worldwide basis. Licenses related to the VY-AADC Program terminated in August 2021.

As a result of the June 2019 Sanofi Genzyme Termination Agreement, we gained worldwide rights to the Huntington's disease program for VY-HTT01 and ex-U.S. rights to the FA program. We subsequently transferred the ex-U.S. rights to the FA Program to Neurocrine pursuant to the 2019 Neurocrine Collaboration Agreement. To facilitate our transfer of the ex-U.S. rights to the FA Program to Neurocrine, we and Neurocrine amended the 2019 Neurocrine Collaboration Agreement and we received a $5.0 million payment from Neurocrine.

Pursuant to development plans to be agreed by the parties, which are overseen by a joint steering committee, or JSC, we have operational responsibility, subject to certain exceptions, for the conduct of each 2019 Neurocrine Program prior to the Transition Event for each Program, as described below, and are required to use commercially reasonable efforts to develop the 2019 Collaboration Products. Neurocrine has agreed to be responsible for all costs incurred by us in conducting these activities for each 2019 Neurocrine Program, in accordance with an agreed budget. If we breach our development responsibilities or in certain circumstances upon a change in control of us, Neurocrine has the right but not the obligation to assume the activities under such 2019 Neurocrine Program.

Upon the occurrence of a specified event for each 2019 Neurocrine Program, or a 2019 Transition Event, Neurocrine agreed to assume responsibility for development, manufacturing and commercialization activities for such

2019 Neurocrine Program from us and to pay milestones and royalties on future net sales as described further below. For each Legacy Program, we were granted the option, or a 2019 Co-Co Option, to co-develop and co-commercialize such 2019 Neurocrine Program upon the occurrence of a specified event, or a 2019 Co-Co Trigger Event. We agreed, upon our exercise of a 2019 Co-Co Option, to enter into a cost- and profit-sharing arrangement with Neurocrine, or a 2019 Co-Co Agreement, and (a) jointly develop and commercialize 2019 Collaboration Products for such 2019 Neurocrine Program, or 2019 Co-Co Products, (b) share in its costs, profits and losses, and (c) forfeit certain milestones and royalties on net sales in the United States during the effective period of the applicable 2019 Co-Co Agreement. The 2019 Co-Co Option has expired, and the 2019 Transition Event and the 2019 Co-Co Trigger Event are no longer applicable, with respect to the VY-AADC Program in light of the termination of the 2019 Neurocrine Collaboration Agreement with respect to the program. The remaining 2019 Transition Events are (a) with respect to the FA Program, our receipt of topline data for the initial Phase 1 clinical trial for an FA Program product candidate; and (b) with respect to each 2019 Discovery Program, the preparation by us and the approval by Neurocrine of an IND application to be filed with the FDA by Neurocrine for the first development candidate in such 2019 Discovery Program. The 2019 Co-Co Trigger Event for the FA Program is the achievement of milestones or metrics specified in the applicable development plan, as determined by the JSC.

Under the 2019 Neurocrine Collaboration Agreement, subject to exceptions specified, we and Neurocrine agreed that profits and losses under our 2019 Co-Co Option would be allocated (a) 50% to Neurocrine and 50% to us for a 2019 Collaboration Product from the VY-AADC Program and (b) 60% to Neurocrine and 40% to us for a 2019 Collaboration Product from the FA Program; provided, however, that Neurocrine would have the right to elect, within a specified period following the acceptance for filing of a biologics license application, or BLA, from the FDA, to pay a $35.0 million rate-shifting fee to us to change the allocation for the VY-AADC Program to 55% to Neurocrine and 45% to us. The parties agreed that each 2019 Co-Co Agreement would provide us the right to terminate for any reason upon prior written notice to Neurocrine and Neurocrine the right to terminate in certain circumstances upon our change of control.

Governance

Our research and development activities under the 2019 Neurocrine Collaboration Agreement are to be conducted pursuant to plans agreed to by the parties, on a program-by-program basis, and overseen by the JSC, which is composed of an equal number of representatives from the parties. The JSC may delegate matters within its authority to subcommittees of the JSC. In addition, the 2019 Neurocrine Collaboration Agreement establishes working groups to handle specified matters on a subject matter-by-subject matter basis. If a working group or subcommittee cannot agree on a matter within its purview within a specified time, such matter is to be referred sequentially to the JSC and then the executive officers of the parties. If the executive officers are not able to resolve the matter, then (a) with respect to each Legacy Program, subject to specified exceptions, (x) Neurocrine has the right to resolve such matter prior to our exercise of our 2019 Co-Co Option with regard to such 2019 Co-Co Product or if such 2019 Co-Co Option expires or goes unexercised and (y) following the timely exercise by us of our 2019 Co-Co Option, depending on the subject of such matter, either Neurocrine, in certain instances, or the parties jointly or the JSC, in other instances, would have the right to resolve such matter, and (b) with respect to 2019 Discovery Programs, subject to specified exceptions, Neurocrine has the right to resolve such matter.

Candidate Selection

The parties have committed to agree on a list of up to eight target genes, or Targets, from which Neurocrine has the right to nominate Targets for the two 2019 Discovery Programs. The Targets nominated for the 2019 Discovery Programs must be approved by a consensus of the JSC or the executive officers.

Manufacturing

Prior to the 2019 Transition Event for a 2019 Neurocrine Program, we are responsible for the manufacture of any 2019 Collaboration Products for the 2019 Neurocrine Program. Following the Transition Event, the parties shall negotiate the manufacturing and supply responsibilities, subject to the terms of any applicable 2019 Co-Co Agreement.

Financial Terms

Under the terms of the 2019 Neurocrine Collaboration Agreement, Neurocrine has paid us an upfront payment of $115.0 million. In connection with the 2019 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. The 2019 Neurocrine Collaboration Agreement provides for aggregate development milestone payments from Neurocrine to us for 2019 Collaboration Products under (a) the VY-AADC Program of up to $170.0 million, which we are no longer eligible to receive in light of the partial termination of the 2019 Neurocrine Collaboration Agreement; (b) the FA Program of up to $195.0 million, and (c) each of the two 2019 Discovery Programs of up to $130.0 million per 2019 Discovery Program. We may be entitled to receive aggregate commercial milestone payments for each 2019 Collaboration Product of up to $275.0 million, subject to an aggregate cap on commercial milestone payments across all 2019 Neurocrine Programs of $1.1 billion.

Neurocrine has also agreed to pay us royalties, based on future net sales of the 2019 Collaboration Products. Such royalty percentages, for net sales in and outside the United States, as applicable, range (a) for the VY-AADC Program, from the mid-teens to thirty and the low-teens to twenty, respectively, which we are no longer eligible to receive in light of the partial termination of the 2019 Neurocrine Collaboration Agreement; (b) for the FA Program, from the low-teens to high-teens and high-single digits to mid-teens, respectively; and (c) for each 2019 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 2019 Collaboration Product and terminate on the later of (x) the expiration of the last patent covering the 2019 Collaboration Product or its method of use in such country, (y) 10 years from the first commercial sale of the 2019 Collaboration Product in such country and (z) the expiration of regulatory exclusivity in such country, or the 2019 Royalty Term. Royalty payments may be reduced by up to 50% in specified circumstances, including expiration of patents rights related to a 2019 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 2019 Collaboration Product. Additionally, the licenses granted to Neurocrine shall automatically convert to fully paid-up, non-royalty bearing, perpetual, irrevocable, exclusive licenses on a country-by-country and product-by-product basis upon the expiration of the 2019 Royalty Term applicable to such 2019 Collaboration Product in such country.

Intellectual Property

Under the terms of the 2019 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.

Exclusivity

During the term of the 2019 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 2019 Collaboration Product is directed, subject to specified exceptions, including the parties' conduct of basic research activities.

Termination

Unless earlier terminated, the 2019 Neurocrine Collaboration Agreement expires on the later of (a) the expiration of the last to expire 2019 Royalty Term with respect to a 2019 Collaboration Product in all countries in the relevant territory or (b) the expiration or termination of all 2019 Co-Co Agreements. Neurocrine may terminate the 2019 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 2019 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 2019 Collaboration Product to which the termination applies. We may terminate the 2019 Neurocrine Collaboration Agreement, subject to specified conditions, if Neurocrine challenges the validity or

enforceability of certain of our intellectual property rights. Subject to a cure period, either party may terminate the 2019 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 us 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 us with respect to a 2019 Neurocrine Program, if such termination were to occur after a 2019 Transition Event, then (a) if a 2019 Co-Co Agreement is in effect with respect to such program, Neurocrine can terminate the 2019 Co-Co Agreement for such program and we would no longer have co-development and co-commercialization rights with respect to the 2019 Collaboration Product and (b) subject to any license agreements, Neurocrine would no longer have any obligations with respect to any 2019 Collaboration Products resulting from such program.

On February 2, 2021, Neurocrine notified us that it had elected to terminate the 2019 Neurocrine Collaboration Agreement solely with regards to the VY-AADC Program, effective as of the Neurocrine VY-AADC Program Termination Effective Date. The 2019 Neurocrine Collaboration Agreement remains in full force and effect for each other program thereunder. As a result of the termination, as of the Neurocrine VY-AADC Program Termination Effective Date, the license granted by us to Neurocrine thereunder regarding the VY-AADC Program expired and we regained worldwide intellectual property rights regarding the VY-AADC Program.

2023 Neurocrine Collaboration Agreement

On January 8, 2023, we entered into the 2023 Neurocrine Collaboration Agreement for the research, development, manufacture and commercialization of the 2023 Neurocrine Programs.

Collaboration and License

Under the 2023 Neurocrine Collaboration Agreement, we and Neurocrine have agreed to collaborate on the conduct of the 2023 Neurocrine Programs. The 2023 Neurocrine Collaboration Agreement became effective upon the expiration of all applicable waiting periods under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, which occurred on February 21, 2023, or the Neurocrine Effective Date. Under the terms of the 2023 Neurocrine Collaboration Agreement, subject to the rights retained by us thereunder, we granted to Neurocrine, as of the Neurocrine Effective Date, an exclusive, royalty-bearing, sublicensable, worldwide license, under certain of our intellectual property rights, to research, develop, manufacture and commercialize gene therapy products, or the 2023 Collaboration Products, arising under the 2023 Neurocrine Programs.

Pursuant to mutually-agreed development plans, during the period beginning on the Neurocrine Effective Date and ending on the third anniversary of the Neurocrine Effective Date, which period may be extended upon mutual written agreement of us and Neurocrine, or the 2023 Discovery Period, and as overseen by the JSC that oversees our ongoing collaboration with Neurocrine, we are responsible for identifying capsids meeting target criteria, producing development candidates, and conducting other non-clinical activities regarding the 2023 Collaboration Products. Neurocrine has agreed to be responsible for all costs we incur in conducting non-clinical development activities for each 2023 Neurocrine Program, in accordance with an agreed budget. If we breach our development responsibilities or, in certain circumstances, upon a change of control, Neurocrine has the right, but not the obligation, to assume the conduct of our activities under such 2023 Neurocrine Program.

We have been granted the option, or a 2023 Co-Co Option, to co-develop and co-commercialize 2023 Collaboration Products in the GBA1 Program in the United States upon the occurrence of a specified event, or a 2023 Co-Co Trigger Event. Should we elect to exercise our 2023 Co-Co Option, we and Neurocrine agree to enter into a cost- and profit-sharing arrangement, or a 2023 Co-Co Agreement, whereby we and Neurocrine agree to jointly develop and commercialize 2023 Collaboration Products in the GBA1 Program, or 2023 Co-Co Products, in the United States and share equally in the GBA1 Program's costs, profits and losses in the United States, with each party entitled to or responsible for 50% of profits and losses with respect to each 2023 Co-Co Product in the United States, subject to specified exceptions. The parties have agreed that the 2023 Co-Co Agreement will provide us the right to terminate the

2023 Co-Co Agreement for any reason upon prior written notice to Neurocrine and provide Neurocrine the right to terminate or amend the 2023 Co-Co Agreement upon a change of control under certain circumstances. In the event we exercise our 2023 Co-Co Option, the parties have also agreed that Neurocrine is entitled to receive (in addition to its 50% share of profits) 50% of our share of profits until our obligation to repay 50% of all development costs incurred by Neurocrine in connection with the GBA1 Program prior to such exercise have been paid off out of such 50% of our share of profits. The 2023 Co-Co Trigger Event is the date on which we receive topline data from the first Phase 1 clinical trial for a product candidate being developed pursuant to the GBA1 Program.

Governance

Our research and development activities under the 2023 Collaboration Agreement are to be conducted pursuant to plans agreed to by the parties, on a 2023 Neurocrine Program-by-2023 Neurocrine Program basis, and overseen by the JSC, which is composed of an equal number of representatives from each of us and Neurocrine. The JSC may delegate matters within its authority to subcommittees of the JSC. In addition, the 2023 Collaboration Agreement establishes working groups to handle specified matters on a subject matter-by-subject matter basis. If a working group or subcommittee cannot agree on a matter within its purview within a specified time, such matter is to be referred sequentially to the JSC and then the executive officers of the parties. If the executive officers are not able to resolve the matter, then (a) with respect to the GBA1 Program, subject to specified exceptions, (x) Neurocrine has the right to resolve such matter prior to our exercise of our 2023 Co-Co Option for the GBA1 Program or in the event we elect not to exercise our 2023 Co-Co Option, and (y) following the exercise by us of our 2023 Co-Co Option for the GBA1 Program, depending on the subject of such matter, either Neurocrine, in certain instances, or the parties jointly or the JSC, in other instances, would have the right to resolve such matter, and (b) with respect to the 2023 Discovery Programs, subject to specified exceptions, Neurocrine has the right to decide any unresolved matters relating to a 2023 Discovery Program that are within the JSC's authority.

Candidate Selection

Either party may notify the JSC of any gene therapy product candidate that includes a Voyager capsid and a payload that is being developed under a 2023 Neurocrine Program, or a Collaboration Candidate, that it desires to nominate as a development candidate. In such event, the JSC shall determine whether such nominated Collaboration Candidate meets certain development criteria. There will be a maximum of four potential development candidates for which development is being performed under any 2023 Neurocrine Program at any given time during the 2023 Discovery Period. If a Collaboration Candidate fails to meet criteria established by the JSC and is removed from consideration to become a development candidate or is named a development candidate, then a new Collaboration Candidate may be nominated to be a potential development candidate to replace the Collaboration Candidate that has failed or succeeded such that not more than four potential development candidates per program are under consideration at any one time during the 2023 Discovery Period.

Manufacturing

The parties have agreed that the applicable development plans shall specify the allocation between us and Neurocrine of responsibilities for the manufacturing of Collaboration Candidates associated with the applicable 2023 Neurocrine Program during the 2023 Discovery Period. In accordance with the 2023 Collaboration Agreement, the parties have also agreed that, if we conduct any portion of the manufacturing of a Collaboration Candidate, the applicable development plan shall include an obligation for us to assist with the technology transfer of such manufacturing responsibilities to Neurocrine or a third-party contract manufacturing organization, as reasonably requested by Neurocrine, on terms to be mutually-agreed by us and Neurocrine. Following the end of the 2023 Discovery Period, Neurocrine shall be responsible for the manufacturing of all Collaboration Candidates and products

Financial Terms

Under the terms of the 2023 Neurocrine Collaboration Agreement, Neurocrine paid us an upfront payment of approximately $136.0 million and approximately $39.0 million as consideration for an equity purchase of 4,395,588 shares of our common stock in February 2023. The 2023 Collaboration Agreement provides for aggregate development

milestone payments from Neurocrine to us for 2023 Collaboration Products under (a) the GBA1 Program of up to $985.0 million; and (b) each of the three 2023 Discovery Programs of up to $175.0 million for each 2023 Discovery Program. We may be entitled to receive aggregate commercial milestone payments for up to two 2023 Collaboration Products under the GBA1 Program of up to $950.0 million per 2023 Collaboration Product and for one 2023 Collaboration Product under each 2023 Discovery Program of up to $275.0 million per 2023 Discovery Program.

Neurocrine has also agreed to pay us tiered royalties, based on future net sales of the 2023 Collaboration Products. Such royalty percentages, for net sales in and outside the United States, range from (a) for the GBA1 Program, the low double-digits to twenty and the high single-digits to mid-teens, respectively, and (b) for each 2023 Discovery Program, high single-digits to mid-teens and mid-single digits to low double-digits, respectively. On a country-by-country and 2023 Neurocrine Program-by-2023 Neurocrine Program basis, the parties have agreed royalty payments would commence on the first commercial sale of a 2023 Collaboration Product in such country and terminate upon the latest of (a) the expiration, invalidation or the abandonment of the last patent covering the composition of the 2023 Collaboration Product or its approved method of use in such country, (b) ten years from the first commercial sale of the 2023 Collaboration Product in such country and (c) the expiration of regulatory exclusivity in such country, or the 2023 Royalty Term. Royalty payments may be reduced by up to 50% in specified circumstances, including expiration of patent rights related to a 2023 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 2023 Collaboration Product. Additionally, the licenses granted to Neurocrine shall automatically convert to a fully-paid, perpetual, irrevocable royalty-free license on a country-by-country and 2023 Collaboration Product-by-2023 Collaboration Product basis upon the expiration of the 2023 Royalty Term applicable to the 2023 Collaboration Product in such country.

Intellectual Property

Under the terms of the 2023 Neurocrine Collaboration Agreement, each party owns all right, title and interest in and to all patent rights or know-how controlled by such party and existing as of or before the Neurocrine Effective Date or created or acquired solely by or on behalf of such party (including through its or its affiliate's representatives) after the Neurocrine Effective Date outside of its activities under the 2023 Neurocrine Collaboration Agreement. The parties have further agreed that all know-how created by either or both parties in the performance of the activities as undertaken pursuant to a development plan during the 2023 Discovery Period or in the course of development, manufacture and commercialization of Collaboration Candidates or products and all patent rights covering such know-how, or collectively the 2023 Arising IP, is to be owned as follows: (a) we solely own all 2023 Arising IP created jointly by representatives of us and Neurocrine that constitutes capsid know-how and capsid patent rights, and 2023 Arising IP created solely by representatives of Neurocrine through the use of our confidential information, including unpublished sequence information for our capsids; and (b) with respect to all other 2023 Arising IP, (x) we solely own all such 2023 Arising IP created solely by its representatives, (y) Neurocrine solely owns all such 2023 Arising IP created solely by its representatives; and (z) the parties jointly own all such 2023 Arising IP created jointly by representatives of both Neurocrine and us. 2023 Arising IP owned by us is included in the license granted from us to Neurocrine described above.

Exclusivity

During the term of the 2023 Neurocrine Collaboration Agreement, neither party nor any of its respective affiliates is permitted to directly or indirectly develop, manufacture or commercialize any other gene therapy product directed to a target under any 2023 Neurocrine Program, or grant any affiliate or third-party a license or sublicense to enable any third-party to do so, subject to specified exceptions, including the parties' conduct of certain basic research, provided that Neurocrine or its affiliates may develop competitive products that do not contain an adeno-associated virus as the viral vector.

Termination

Unless earlier terminated, the 2023 Neurocrine Collaboration Agreement expires on the later of (a) the expiration of the last to expire 2023 Royalty Term with respect to all 2023 Collaboration Products worldwide or (b) the expiration or termination of any 2023 Co-Co Agreement. Neurocrine may terminate the 2023 Neurocrine Collaboration

Agreement in its entirety or on a 2023 Neurocrine Program-by-2023 Neurocrine Program and/or country-by-country basis by providing at least (a) 180-day advance notice if such notice is provided prior to the first commercial sale of any 2023 Collaboration Product to which the termination applies or (b) one-year advance notice if such notice is provided after the first commercial sale of any product to which the termination applies. Neurocrine may terminate the 2023 Neurocrine Collaboration Agreement with respect to a given 2023 Collaboration Product by providing written notice of termination to us within thirty days after complete readout of any clinical trial if the results of such clinical trial fail to meet the pre-specified primary endpoint(s) set forth in the applicable protocol or if there is a safety finding during the clinical trial relating to such 2023 Collaboration Product that either (a) is substantially irreversible or not monitorable in patients or (b) results in Neurocrine's decision to designate such 2023 Collaboration Product as a terminated product under the 2023 Collaboration Agreement.

We may terminate the 2023 Neurocrine Collaboration Agreement with respect to a particular patent right of ours, if Neurocrine challenges the validity or enforceability of such patent right. Subject to a cure period, either party may terminate the 2023 Neurocrine Collaboration Agreement in the event of a material breach in whole or in part, subject to specified conditions.

2023 Neurocrine Stock Purchase Agreement

In connection with the execution of the 2023 Neurocrine Collaboration Agreement, Neurocrine and the Company also entered into a stock purchase agreement on the January 8, 2023 for the sale and issuance of 4,395,588 shares of common stock to Neurocrine at a price of $8.88 per share, for an aggregate purchase price of approximately $39.0 million. In accordance with the terms and conditions of the stock purchase agreement, we issued and sold these shares to Neurocrine on February 23, 2023.

2023 Neurocrine Amended and Restated Investors Rights Agreement

In connection with the execution of the 2023 Neurocrine Collaboration Agreement, Neurocrine and the Company also amended and restated their existing investor agreement on January 8, 2023, or the 2023 Neurocrine Amended and Restated Investor Agreement, providing for standstill and lock-up restrictions and a voting agreement with respect to shares of the Company owned by Neurocrine. Pursuant to the 2023 Neurocrine Amended and Restated Investor Agreement, the Company caused Jude Onyia, Ph.D., Chief Scientific Officer of Neurocrine, to be appointed to the Company's board of directors as a Class III director on February 23, 2023. The Company has agreed that it shall cause Dr. Onyia, or another individual designated by Neurocrine, to be nominated for election to the Company's board of directors when Dr. Onyia's initial term is scheduled to expire. Under the 2023 Neurocrine Amended and Restated Investor Agreement, Neurocrine's right to designate an individual to serve as a director on the Company's board of directors and the Company's agreement to nominate such individual for election to the Company's board of directors is subject to specified conditions and shall terminate upon the earliest of (a) Neurocrine holding less than 10% of the Company's outstanding common stock; (b) a change of control of the Company or Neurocrine; (c) a liquidation or dissolution of the Company; and (iv) the date that is ten years from the closing date of the 2023 Neurocrine Amended and Restated Investor Agreement.

Pursuant to the terms of the 2023 Neurocrine Amended and Restated Investor Agreement, Neurocrine has agreed not to, without the prior written approval of the Company and subject to specified conditions, directly or indirectly acquire shares of the Company's outstanding common stock, seek or propose a tender or exchange offer or merger between the parties, solicit proxies or consents with respect to any matter, or undertake other specified actions related to the potential acquisition of additional equity interests in the Company (the "Standstill Restrictions"). Further, Neurocrine has also agreed not to, and to cause its affiliates not to, sell or transfer any shares of the Company without the prior written approval of the Company, subject to specified conditions (the "Lock-Up Restrictions").

In addition, pursuant to the terms of the 2023 Neurocrine Amended and Restated Investor Agreement, Neurocrine has agreed that any shares of the Company it owns are subject to a voting agreement such that, subject to specified conditions and excluding specified extraordinary matters, Neurocrine has agreed to, and has agreed to cause its permitted transferees to, vote in accordance with the recommendation of the Company's board of directors and has granted the Company an irrevocable proxy with respect to the foregoing (the "Voting Agreement").

Each of the Standstill Restrictions, the Lock-Up Restrictions, and the Voting Agreement terminate upon the earliest to occur of: (i) the date that is the third anniversary of the effective date of the 2023 Neurocrine Amended and Restated Investor Agreement and (ii) a liquidation or dissolution of the Company. The Standstill Restrictions and Lock-Up Restrictions also terminate upon the deregistration of the Company's common stock, if earlier. The Lock-Up Restrictions and Voting Agreement also terminate on a change of control of the Company or the date on which Neurocrine and its affiliates beneficially own less than three percent of the common stock of the Company on an outstanding basis. The Standstill Restrictions and Voting Agreement also terminate upon the later of (x) the expiration or termination of the 2019 Neurocrine Collaboration Agreement and (y) the expiration or termination of the 2023 Neurocrine Collaboration Agreement.

License Agreement with Touchlight IP Limited

In November 2022, we and Touchlight entered into the Touchlight License Agreement, to authorize historical use by us of a certain DNA preparation process, or the Subject DNA Preparation Process, and to authorize the prospective exploitation of TRACER capsids created with the use of the Subject DNA Preparation Process.

The terms of the Touchlight License Agreement include a one-time, non-refundable technology access fee of $5.0 million, paid to Touchlight during the fourth quarter of 2022.

The terms of the Touchlight License Agreement also include future milestone payments and low single-digit royalties payable to Touchlight by us if we or our program collaborators or licensees choose to utilize in a therapeutic product TRACER capsids that were created with the historical use of the Subject DNA Preparation Process. Additionally, we are obligated to pay low single-digit royalties to Touchlight on future payments we receive in connection with licensing of TRACER capsids that were created with the historical use of the Subject DNA Preparation Process, excluding the licensing of or collaboration on any of our therapeutic programs.

Competition

The biopharmaceutical industry is characterized by intense and dynamic competition to develop new technologies and proprietary therapies. Any product candidates that we successfully develop into products and commercialize may compete with existing therapies and new therapies that may become available in the future. While we believe that our gene therapy platform, product programs, product candidates and scientific expertise in the fields of gene therapy and neuroscience provide us with competitive advantages, we face potential competition from various sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, governmental agencies and public and private research institutions.

We are aware of several companies focused on developing AAV gene therapies in various indications, including AavantiBio, Inc. (acquired by Solid Biosciences, Inc., or Solid), Abeona Therapeutics, Inc., Adverum Biotechnologies, Inc., Aevitas Therapeutics, Inc., Akuous, Inc. (acquired by Eli Lilly and Company, or Eli Lilly), Alcyone Therapeutics, Inc., Amicus Therapeutics, Inc., Apic Bio, Inc., Applied Genetic Technologies Corporation (acquired by Syncona Limited), 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), BioMarin Pharmaceuticals, Inc., Encoded Therapeutics, Inc., GenSight Biologics SA, Homology Medicines, Inc., LEXEO Therapeutics, Inc., LogicBio Therapeutics, Inc. (acquired by AstraZeneca), Lysogene SA, MeiraGTx Ltd., or MeiraGTx, Neurogene, Inc., Novartis Gene Therapies, Inc. (formerly AveXis, Inc.), Passage Bio, Inc., Pfizer, Inc., Prevail Therapeutics, Inc. (acquired by Eli Lilly), PTC Therapeutics, Inc., or PTC, REGENXBio Inc., Sarepta Therapeutics, Inc., Solid, Spark Therapeutics, Inc. (acquired by Roche), 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 discovery platform and preclinical programs will compete with a variety of 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), Freeline Therapeutics Holdings plc, Pfizer, Biogen, Lysogene SA, and Coave Therapeutics SA;

- Our program for tauopathies including AD, 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, AbbVie Biotechnology Ltd, AbbVie Ireland Unlimited Company, 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 Tofersen being developed by Biogen, in collaboration with Ionis, and gene therapies being developed by Novartis Gene Therapies, Inc. and Apic Bio, Inc.; and

- Our FA Program will potentially compete with AAV gene therapies being developed by LEXEO Therapeutics, Inc., AavantiBio, Inc. (acquired by Solid), PTC, StrideBio, Inc. in collaboration with Takeda Pharmaceutical Company Limited, Pfizer, and Novartis Gene Therapies, Inc.

Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of product candidates and commercializing those product candidates. Accordingly, our competitors may be more successful than us in obtaining approval for product candidates and achieving widespread market acceptance. Our competitors' product candidates may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our treatments obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates.

Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

We anticipate that we will face intense and increasing competition as new product candidates enter the market and advanced technologies become available. We expect any product candidates that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, and the availability of reimbursement from government and other third-party payers.

Our commercial opportunity could be reduced or eliminated if our 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. Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Manufacturing

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 HEK 293 cell manufacturing to support our preclinical research activities. We also have expertise with the baculovirus/Sf9 AAV production system, a technology for producing AAV vectors at scale in insect-derived cells, which we have used for our clinical development activities in the past and may use in the future for clinical development activities. We focus on developing internal processes and capabilities to produce high-yield and high-quality gene therapies. Both the HEK 293 cell manufacturing process and the baculovirus/Sf9 manufacturing process have been successfully transferred to our contract manufacturing organizations. The baculovirus/Sf9 manufacturing process has been used by our contract manufacturing organizations in manufacturing of clinical materials in accordance with the FDA's current good manufacturing practices, or cGMPs. We have also built an onsite, state-of-the-art process research and development facility to enable the manufacturing of high quality AAV gene therapy vectors at research scale.

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

Intellectual Property

Overview

We strive to protect the proprietary technology, inventions, and know-how to enhance improvements that are commercially important to the development of our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets and know-how relating to our proprietary technology platform, on continuing technological innovation and on in-licensing opportunities to develop, improve and maintain the strength of our position in the field of gene therapy that may be important for the development of our business. We additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available.

Our commercial success may depend in part on our ability to: obtain and maintain patent and other protections for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and intellectual property rights of third parties. Our ability to stop third parties from making, having made, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable licenses, patents or trade secrets that cover these activities. In some cases, these rights may need to be enforced by third-party licensors. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same.

We own at least 390 pending patent applications and at least 54 patents have issued in the United States and foreign jurisdictions. We co-own at least 43 pending patent applications and at least 10 patents have issued from these co-owned families in the United States and foreign jurisdictions. At least 12 patent applications have been filed and are pending in the United States and foreign jurisdictions by or on behalf of universities which have granted us exclusive license rights to the technology. To date, at least 44 patents have issued to our licensors which have granted us exclusive license rights to the technology. To date, at least 148 patents have issued to our licensors which have granted us non-exclusive license rights to the technology with at least 68 applications pending. Our policy is to file patent applications to protect technology, inventions and improvements to inventions that are commercially important to the development of our business. We seek United States and international patent protection for a variety of technologies, including: AAV-

based biological products and constructs, methods of delivering said AAV-based biological products and constructs, methods of treating diseases of interest, as well as methods of engineering and manufacturing of the same. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel biological products. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various other license agreements that give us rights to use specific technologies in our research and development.

Company-Owned Intellectual Property

Parkinson's Disease

We own three pending patent families with four issued patents and 35 patent applications directed to AAV constructs encoding the gene AADC for therapeutic uses. Patents that grant from these patent families are generally expected to commence expiration in 2035, subject to possible patent term extensions.

Huntington's Disease

We own five pending patent families with three issued patents and 29 patent applications directed to pharmaceutical compositions and methods for targeting HTT for the treatment of Huntington's disease. Patents from this family are generally expected to commence expiration in 2037, with some applications expiring in 2038, 2040, and 2044 all of which are subject to possible patent term extensions.

ALS

We own five pending patent families and have nine issued patents and 34 patent applications directed to targeting SOD1 for the treatment of ALS. We co-own a sixth patent family with eight pending patent applications directed to pharmaceutical compositions and methods for the treatment of ALS to protect our intellectual property arising from a funded grant from The Amyotrophic Lateral Sclerosis Association. We own one pending patent family with one patent application directed to chromosome 9 open reading frame 72, or C9orf72, for the treatment of ALS. Patents that grant from these patent families are generally expected to commence expiration in 2035, with some applications expiring in 2038, 2039, 2040, and 2042, all of which are subject to possible patent term extensions.

Friedreich's Ataxia

We own three pending patent families with 23 patent applications and we co-own one pending patent family with eight patent applications directed to AAVs encoding frataxin constructs for the treatment of Friedreich's ataxia. Patents that grant from these patent families are generally expected to commence expiration in 2036, with some later filed applications commencing expiration in 2038, 2039, and 2040, all of which are subject to possible patent term extensions.

GBA1 Gene Therapy

We own two pending patent families with 14 pending patent applications directed to AAVs encoding GBA1 for the treatment of Parkinson's disease, Gaucher disease, and dementia with Lewy Bodies. Patents that grant from this patent family are expected to commence expiration in 2041 and 2043, subject to possible patent term extensions.

Vectorized Antibodies

We own four patent families with two issued patents and eight pending patent applications directed to vectorized antibodies and related platforms. Patents that grant from these patent families are generally expected to commence expiration in 2037, with some later filed applications commencing expiration in 2040, all of which are subject to possible patent term extensions.

Tauopathies

We own seven pending patent families directed to antibodies to tau and vectorized forms thereof with 26 pending patent applications. Patents that grant from these families are generally expected to commence expiration in 2037, with some later filed applications commencing expiration in 2040, 2041, 2042, and 2043 all of which are subject to possible patent term extensions. We own one pending patent family to RNA inhibitors for treating tauopathies. Patents that grant from this family are generally expected to commence expiration in 2043, subject to possible patent term extensions.

We have one pending patent family with one pending patent applications directed to pharmaceutical compositions and methods for the treatment of AD. Patents that grant from this family are generally expected to commence expiration in 2043, subject to possible patent term extensions.

Vectorized anti-HER2

We own one pending patent family with one pending patent application directed to AAVs encoding HER2 antibodies for treating metastatic HER2 positive cancers. Patents that grant from these patent families are generally expected to commence expiration in 2042, subject to possible patent term extensions.

Regulatable Expression

We own one pending patent family with three pending patent applications directed to regulatable expression control of AAV transgenes. Patents that grant from this patent family are generally expected to commence expiration in 2036, subject to possible patent term extensions.

Delivery

We own one pending patent family with one patent application directed to cannula delivery system and methods of use. Patents that grant from this patent family are generally expected to commence expiration in 2039, subject to possible patent term extensions.

We co-own two pending patent families directed to trajectory array delivery devices, including the variable trajectory array guide, or V-TAG®, device and methods of use. The first pending patent family has one granted patent and six pending patent applications, and the second pending patent family has one granted patent and six pending patent applications. Patents that grant from these patent families are generally expected to commence expiration in 2037 and 2038, subject to possible patent term extensions.

Capsids

We own two patent families pending in the United States and foreign jurisdictions that are directed to the TRACER discovery platform for selection of AAV capsids with BBB crossing and cell-specific transduction properties. In these two pending patent families directed to the TRACER discovery platform, there are 10 applications pending, and are generally expected to commence expiration in 2039 and 2041, respectively, subject to possible patent term extensions. We also own four pending patent families comprising 34 non-provisional, United States and foreign applications, as well as three pending provisional applications directed to capsid variants identified using the TRACER discovery platform showing improved properties over AAV9. Patents that grant from these patent families and pending provisional applications are generally expected to commence expiration in 2041, 2042 and 2043, subject to possible patent term extensions. We own two pending provisional applications and three pending non-provisional applications directed to constructs containing TRACER capsids in combination with specific payloads for treatment of CNS and other indications. Patents that grant from these pending provisional and non-provisional applications are generally expected to commence expiration in 2042 and 2043, subject to possible patent term extensions.

We also own five patent families pending in the United States and foreign jurisdictions directed to capsid variants generated using other methodologies. In these five pending patent families, there are two granted patents and 20

pending patent applications. Patents that grant from these patent families are generally expected to commence expiration in 2038, subject to possible patent term extensions. We also co-own three patent families directed to other capsid variants. In these three pending patent families there are five pending applications. Patents that grant from these patent families are generally expected to commence expiration in 2039 and 2040, subject to possible patent term extensions.

Vector and Genome Engineering

We own three patent families with 32 issued patents (including 15 patents in European countries) and 45 patent applications directed to engineering of the vector genome. Patents that grant from these patent families are generally expected to commence expiration in 2035, 2037, and 2038, which are all subject to possible patent term extensions.

We own one patent family with one patent application directed to genome engineering. Patents that grant from this patent family are generally expected to commence expiration in 2040, subject to possible patent term extensions.

Production; Chemistry, Manufacturing, and Controls

We own 21 pending patent families with two granted patents and 83 pending patent applications directed to AAV production and CMC. Patents that grant from the earliest filed patent families are generally expected to commence expiration in 2035 and patents that grant from the latest filed patent families are generally expected to commence expiration in 2042, all of which are subject to possible patent term extensions. We co-own one pending patent family with eight granted patent and 11 pending patent applications directed to AAV production and CMC. Patents that grant from this patent family are generally expected to commence expiration in 2037, subject to possible patent term extensions.

Licensed Intellectual Property

We have obtained exclusive licenses and non-exclusive licenses to patents directed to both compositions of matter and methods of use.

We have licensed six families of patents and patent applications, in the field of gene therapy for human diseases, directed to RNAi constructs as vector payloads, their design and use in the treatment of neurological disorders from the University of Massachusetts. Three of the six families of patents and applications are exclusively licensed and comprise 14 granted patents and seven applications in the United States and other territories. Three of the six families of patents and applications are non-exclusively licensed, and comprise 55 granted patents and two applications in the United States and other territories. Patents from these six families have been granted in the United States, Canada, Europe, Israel, Japan, Korea and Australia. Nationalization for some members has taken place in Germany, Spain, France, Great Britain, Italy, and Netherlands. Patents that grant from these patent families are generally expected to expire between 2024 and 2036, subject to possible patent term extensions.

We have exclusively licensed 1 family of patents and patent applications directed to AAV capsids from the University of Massachusetts. In this pending patent family, there are 30 granted patents and six pending patent applications. Patents that grant from this patent family are generally expected to commence expiration in 2030, subject to possible patent term extensions.

We have non-exclusively licensed two pending patent families from Ablexis, LLC. These families of patents and patent applications are pending and/or granted in the United States and other territories and comprise 50 granted patents and 6 applications. Patents have been granted in Australia, Canada, Europe, Korea, New Zealand and the United States. Nationalization for some members has taken place in Austria, Belgium, Denmark, France, Germany, Ireland, Italy, Netherlands, Poland, Spain, Switzerland, and United Kingdom. Patents that grant from these patent families are generally expected to expire between 2029 and 2031, subject to possible patent term extensions.

We have non-exclusively licensed two pending patent families directed to AAV capsids from the California Institute of Technology. These families of patents and patent applications are pending in the United States and internationally and comprise 43 granted patents and 15 applications. Patents have been granted in the United States.

Patents that grant from these patent families are generally expected to commence expiration in 2034 and 2036, subject to possible patent term extensions.

We have non-exclusively licensed three pending patent families directed to microRNA detargeting from the University of Pennsylvania. These families of patent applications are pending in the United States and internationally and comprise 45 applications. Patents that grant from these patent families are generally expected to commence expiration in 2039, 2041, and 2042, subject to possible patent term extensions.

Trademark Protection

We own trademark registrations in the United States for the marks VOYAGER THERAPEUTICS and VOYAGER THERAPEUTICS Logo for "pharmaceutical research and development in the field of gene therapy." We also own pending applications for VOYAGER, and VOYAGER with design elements in the United States, and registrations for VOYAGER with design elements in the European Union and United Kingdom, for goods and services including, among others, "biological preparations for gene therapy," "pharmaceutical research and development in the field of gene therapy," and "medical services provided for clinical trials."

We also own U.S. trademark registrations for the mark V-TAG and the V-TAG Logo, for "medical system comprised of a surgical device for guiding, locating or placing a diagnostic device or therapeutic device, namely, stents, probes, needles, leads, grafts, pumps, syringes, catheters, and implants during a medical procedure and related software sold as a unit, none of the aforesaid for use in cardiac ablation; MRI-compatible medical system comprised of an MRI-compatible surgical device for guiding, locating or placing a diagnostic device or therapeutic device, namely, stents, probes, needles, leads, grafts, pumps, syringes, catheters, and implants during a MRI-guided procedure and related software sold as a unit, none of the aforesaid for use in cardiac ablation," as well as trademark registrations in the European Union and United Kingdom for V-TAG for similar trademark classes.

We also own pending applications in the U.S. and European Union, and a registration in the United Kingdom, for the mark TRACER for services including, among others, "research and development of platform technologies for genetic delivery of therapies and pharmaceutical via adeno-associated virus (AAV) capsids."

We plan to register trademarks in connection with our biological products.

Trade Secret Protection

Finally, we may rely, in some circumstances, on trade secrets to protect our technology. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. 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. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Government Regulation

The research, development, testing, manufacture, quality control, packaging, labeling, storage, record-keeping, distribution, import, export, promotion, advertising, marketing, sale, pricing and reimbursement of biologic products are extensively regulated by governmental authorities in the United States and other countries. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory requirements, both pre-approval and post-approval, require the expenditure of substantial time and financial resources. The regulatory requirements applicable to biological product development, approval and marketing are subject to change, and regulations and administrative guidance often are revised or reinterpreted by the agencies in ways that may have a significant impact on our business.

U.S. Government Regulation

U.S. Biological Products Development Process

In the United States, the FDA approves and regulates gene therapy products as biological products, or biologics. These products are licensed for marketing under the Public Health Service Act, or the PHSA, and regulated under the Federal Food, Drug, and Cosmetic Act, or FDCA. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor.

The process required by the FDA before a biological product may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies according to the FDA's good laboratory practices, or GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- preparation of clinical trial material in accordance with cGMPs;
- design of a clinical protocol and submission to the FDA of an application for an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee representing each clinical trial site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to the FDA's good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety, purity, potency, and efficacy, of the proposed biological product for its intended use;
- submission to the FDA of a BLA for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical studies, including payment of application user fees;
- satisfactory completion of an FDA inspection prior to BLA approval of the manufacturing facility or facilities where the biological product is produced to assess compliance with cGMP, to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;
- potential FDA inspection of the nonclinical and clinical study sites that generated the data in support of the BLA;
- potential FDA Advisory Committee meeting to elicit expert input on critical issues and including a vote by external Committee members;
- FDA review and approval, or licensure, of the BLA; and
- compliance with any post approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post approval studies.

Preclinical Studies

Before a sponsor begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry,

formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. These studies are generally referred to as IND-enabling studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND and are typically referred to as IND-enabling studies. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. An IND must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA or BLA. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial may proceed. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a partial clinical hold might state that a specific protocol or part of a protocol may not proceed, while other parts of a protocol or other protocols may do so. No more than 30 days after the imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following the issuance of a clinical hold or partial clinical hold, a clinical investigation may only resume once the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed or recommence. Occasionally, clinical holds are imposed due to manufacturing issues that may present safety issues for the clinical study subjects.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived by the FDA. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB, which must operate in compliance with FDA regulations, must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects and must monitor the trial until completed. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board, or DSMB. This group provides authorization as to whether or not a trial may move forward at designated checkpoints based on review of available data from the study, to which only the

DSMB maintains access. Suspension or termination of development during any phase of a clinical trial can occur if the DSMB determines that the participants or patients are being exposed to an unacceptable health risk.

Human Clinical Trials

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator in accordance with GCP requirements which include, among other things, the requirement that all research subjects provide their informed consent in writing before they participate in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol, and any subsequent material amendment to the protocol, must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

Phase 1 clinical trials are initially conducted in a limited population, which may be healthy volunteers or subjects with the target disease, to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the product candidate's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are typically well-controlled and closely monitored.

Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken using a larger patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a new biologic product. Such Phase 3 clinical trials are referred to as "pivotal" trials.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Moreover, as noted above, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

In some cases, the FDA may approve an NDA or BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials, typically referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials, such as to verify clinical benefit in the case of products approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting mandatory Phase 4 clinical trials could result in withdrawal of FDA approval for products.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017. Although the FDA has historically not enforced these reporting requirements due to a long delay by the Department of Health and Human Services, or HHS, in issuing final implementing regulations, the FDA has issued several Notices of Noncompliance to manufacturers since April 2021. The failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues.

Gene Therapy Products

We expect that the procedures and standards applied to gene therapy products will be applied to any product candidates we may develop. The FDA has defined a gene therapy product as one that seeks to modify or manipulate the expression of a gene or to alter the biological properties of living cells for therapeutic use. The products may be used to modify cells in vivo or transferred to cells ex vivo prior to administration to the recipient. Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within CBER, the review of gene therapy and related products is consolidated in the Office of Tissues and Advanced Therapies, or OTAT, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The NIH, including the NExTRAC also advises the FDA on gene therapy issues and other issues related to emerging biotechnologies. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols.

The FDA has issued various guidance documents regarding gene therapies, including final guidance documents released in January 2020 relating to chemistry, manufacturing and controls information for gene therapy INDs, long-term follow-up after the administration of gene therapy products, gene therapies for rare diseases and gene therapies for retinal disorders, as well as draft guidance in January 2021 for Human Gene Therapy for Neurodegenerative Diseases. Although the FDA has indicated that these and other guidance documents it previously issued are not legally binding, compliance with them is likely necessary to gain approval for any gene therapy product candidate. The guidance documents provide additional factors that the FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical assessment of gene therapies; the chemistry, manufacturing and control information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe for potential delayed adverse effects in participants who have received investigational gene therapies with the duration of follow-up based on the potential for risk of such effects. For AAV vectors specifically, the FDA typically recommends that sponsors continue to monitor participants for potential gene therapy-related adverse events for up to a five-year period.

Until 2019, most gene therapy clinical trials in the United States required pre-review by the predecessor of NExTRAC before being approved by the IRBs and any local biosafety boards or being allowed to proceed by the FDA. In 2019, the NIH substantially eliminated the pre-review process and going forward, the review of gene therapy clinical trial protocols would be largely handled by local IRBs and institutional biosafety committees, or IBCs, in addition to the FDA. Furthermore, in 2019, the NIH removed from public access the Genetic Modification Clinical Research Information System database, which previously contained substantial amounts of safety and other participant information regarding human gene therapy trials performed up to that time.

Manufacturing and Other Regulatory Requirements

Concurrently with clinical trials, sponsors usually complete additional animal safety studies, develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing commercial quantities of the product candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other criteria, the sponsor must develop methods for testing the identity, strength, quality, and purity of the finished product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside of the United States prior to being imported or offered for import into the United States. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

Submission of a BLA to the FDA

FDA approval is required before any new gene therapy product or dosage form, including a new use of a previously approved gene therapy product, can be marketed in the United States. Thus, assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational gene therapy product information is submitted to the FDA in the form of a BLA requesting approval to market the product for one or more indications. The BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information. Under the Prescription Drug User Fee Act, or PDUFA, each BLA must be accompanied by a significant user fee unless an exception or waiver applies, such as the first application filed by a small business or BLAs for product candidates designated as orphan drugs, unless the product candidate includes an indication that is not for a rare disease or condition.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In pertinent part, FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the sponsor. In this event, the BLA must be resubmitted.

If the submission is accepted for filing, the FDA's goal is to review the BLA, within ten months for a standard review, or, if the BLA relates to an unmet medical need in the treatment of a serious or life-threatening condition, perform a priority review, within six months. The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission. Despite these review goals, it is not uncommon for FDA review of an application to extend beyond the PDUFA target action date.

The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a REMS is necessary to assure the safe use of the biological product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

In connection with its review of a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, the FDA will typically inspect one or more clinical trial sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. With passage of FDORA, Congress clarified the FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to the FDA as well as other persons holding study records or involved in the study process. To assure cGMP and GCP compliance, a sponsor must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

The FDA's Decision on a BLA

The FDA reviews an application to determine, among other things, whether the product is safe, pure and potent for its intended use(s), with the latter determination being made on the basis of substantial evidence. The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish the efficacy of a new product. Under certain circumstances, however, FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter, or CRL, or an approval letter. To reach this determination, the FDA must determine that the expected benefits of the proposed product outweigh its potential risks to patients.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six-month extension to respond. For those seeking to challenge the FDA's CRL decision, the FDA has indicated that sponsors may request a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Gene therapy products manufactured or distributed pursuant to regulatory approvals are subject to pervasive and continuing regulation by the regulatory authorities, including, among other things, requirements relating to formal commitments for post approval clinical trials and studies, manufacturing, recordkeeping, periodic reporting, product sampling and distribution, marketing, labeling, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior regulatory authority review and approval.

Manufacturers are subject to periodic unannounced inspections by regulatory authorities and country or state agencies for compliance with cGMP and other requirements. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior regulatory approval before being implemented. Regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Further, although physicians may prescribe legally available products for unapproved uses or patient populations, which are commonly referred to as "off-label uses," manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. In September 2021, the FDA published final regulations which describe the types of evidence that the FDA will consider in determining the intended use of a biologic. If a company is found to have promoted off-label uses, it may become subject to administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the HHS, as well as state authorities.

It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. Moreover, with passage of the Pre-Approval Information Exchange Act, or PIE Act, in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance, but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products.

Expedited Review Programs

The FDA is authorized to expedite the review of applications in several ways. None of these expedited programs, however, changes the standards for approval but each may help expedite the development or approval process governing product candidates.

- *Fast Track Designation*. Candidate products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.

- *Breakthrough therapy designation*. To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.

- *Priority review*. A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. FDA aims to complete its review of priority review applications within six months as opposed to ten months for standard review.

- *Accelerated approval*. Biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a biologic product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials. With passage of FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to: require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to the FDA every six months until the study is completed; and use expedited procedures to withdraw accelerated approval of an NDA or BLA after the confirmatory trial fails to verify the product candidate's clinical benefit. Further, FDORA requires the FDA to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval.

- *Regenerative advanced therapy*. With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

U.S. Orphan Drug Designation and Exclusivity

A gene therapy product may qualify for orphan drug designation, or ODD, under the Orphan Drug Act, if it is intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product. ODD must be requested before submitting a BLA. After the FDA grants ODD, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. ODD entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. ODD does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a gene therapy product that has ODD receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same gene therapy product for the same indication for seven years, except in limited circumstances, such as not being able to supply the product for patients or showing clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of a different gene therapy for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan-drug exclusivity also could block the approval of one of our products for

seven years if a competitor obtains approval of the same gene therapy as defined by the FDA. 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 the sameness.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

Orphan drug products are also eligible for Rare Pediatric Disease Designation if greater than 50% of patients living with the disease are under age 18. A priority review voucher, or PRV, will be given to the sponsor of a product with a Rare Pediatric Disease Designation at the time of product approval that is transferable to another company. A PRV is a voucher that the FDA issues to a sponsor of a rare pediatric disease or tropical disease product application at the time of the marketing application approval. Vouchers are transferable to other sponsors that may apply it to their new drug applications or BLAs. A PRV entitles the holder to designate a single human drug application submitted under Section 505(b)(1) of the FDCA or Section 351 of the PHSA as qualifying for a priority review. An FDA priority review may expedite the review process of a marketing application reducing the review time from ten months after formal acceptance of the file to six months after formal acceptance of the file. Applying the PRV to a marketing application does not ensure the FDA's approval of the marketing application and all requirements supporting the safety and efficacy of the product must be met.

Biosimilars and Exclusivity

When a biological product is licensed for marketing by FDA with approval of a BLA, the product may be entitled to certain types of market and data exclusivity barring FDA from approving competing products for certain periods of time. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, was enacted in the United States and included the Biologics Price Competition and Innovation Act of 2009, or the BPCIA. The BPCIA amended the PHSA to create an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, the FDA has approved a number of biosimilars and several interchangeable biosimilar products. In December 2022, Congress clarified through FDORA that the FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the first day on which such a product is approved as interchangeable with the reference product.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product. Approval of a 351(k) application may not be made effective until twelve years after the date of first licensure of the reference product, which under the statute excludes the date of licensure of supplements and certain other applications. Additionally, a 351(k) application for a biosimilar or interchangeable biological product cannot be submitted for review until four years after the date on which the reference product was first licensed under section 351(a) of the PHSA. Even if a product is considered to be a reference product eligible for exclusivity, however, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well controlled clinical trials to demonstrate the safety, purity, and potency of their product. There have been recent government proposals to reduce the twelve-year reference product exclusivity period, but none has been enacted to date. At the same time, since passage of the BPCIA, many states have passed laws or amendments to laws, which address pharmacy practices involving biosimilar products.

U.S. Patent Term Restoration

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application, less any time the sponsor failed to act with due diligence. Only one patent applicable to an approved biological product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

Other Healthcare Laws

Although we currently do not have any products on the market, we will be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states in which we conduct our business, if and when our product candidates are approved by the FDA and subject to federal healthcare reimbursement. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations. In addition, the U.S. Foreign Corrupt Practices Act, to which we are subject, prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of biologic products, limiting coverage and reimbursement for medical products and other changes to the healthcare system in the United States. In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for pharmaceutical products under government healthcare programs. The ACA is intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose taxes and fees on the health industry and impose additional health policy reforms. 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. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government healthcare programs. Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, 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 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through 2031 pursuant to the Coronavirus Aid, Relief and Economic Security Act, or

CARES Act. These Medicare sequester reductions were reduced and suspended through the end of June 2022, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, which was enacted in January 2013, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, 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. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%.

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 United States District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TJCA, the remaining provisions of the ACA are invalid as well. The United States Supreme Court heard this case on November 10, 2020 and, on June 17, 2021, dismissed this action after finding that the 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.

Although the previous administration took executive actions to undermine or delay implementation of the ACA, those actions were rescinded with issuance of an Executive Order on January 28, 2021 by President Biden, 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.

Pharmaceutical Price Reform

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent United States congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription products from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of products from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1,

2022, but with passage of the Inflation Reduction Act of 2022, or IRA, it has been delayed by Congress to January 1, 2032.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. To address these costs, the executive order directs HHS to create a plan within 45 days to combat "excessive pricing of prescription drugs and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such drugs, and to address the recurrent problem of price gouging." Thereafter, on September 9, 2021, HHS released its plan to reduce drug prices. The key features of that plan are to: (a) make drug prices more affordable and equitable for all consumers and throughout the health care system by supporting drug price negotiations with manufacturers; (b) improve and promote competition throughout the prescription drug industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the IRA was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription product 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.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our

operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Government Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials, e.g., a clinical trial application for each clinical trial for each EU country in which the trial is conducted; a clinical trial notification is required in Japan.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Our Corporate Information

We were incorporated under the laws of Delaware in June 2013. Our principal executive offices are located at 64 Sidney Street, Cambridge, MA 02139. Other operations, including laboratory space, are located at 75 Hayden Avenue, Lexington, MA. We lease our office and laboratory space, which consist of approximately 26,148 square feet located in Cambridge, Massachusetts and 32,142 square feet located in Lexington, MA. Our lease in Cambridge expires in 2026 and our lease in Lexington expires in 2031.

Employees and Human Capital Resources

As of December 31, 2022, we employed 125 full-time employees in the United States, including 94 in research and development positions and 31 in general and administrative positions. Approximately 40 of our employees have either an MD or PhD degree. We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be positive.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate our employees and directors and selected consultants through the granting of stock-based compensation awards.

Available Information

Our Internet address is http://www.voyagertherapeutics.com. We make available, free of charge, on or through our website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities and Exchange Act as soon as reasonably practicable after such material is electronically filed with or furnished to the Securities and Exchange Commission, or the SEC. The information on our website is not part of this Annual Report for the year ended December 31, 2022.

ITEM 1A. RISK FACTORS

The following risk factors and other information in this Annual Report on Form 10-K, including our 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 the discussion under the caption "Forward-Looking Statements" in this Annual Report on Form 10-K 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 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. We had net losses of $46.4 million and $71.2 million for the year ended December 31, 2022 and December 31, 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $393.5 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, AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company, and our ongoing collaborations with Neurocrine Biosciences, Inc., or Neurocrine; our option and license agreement, or the Pfizer Agreement, with Pfizer Inc., or Pfizer; and our option and license agreement, or the Novartis Agreement, with Novartis Pharma, AG, or Novartis. We refer to our ongoing collaborations with Neurocrine collectively as the Neurocrine Collaborations.

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 ever. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We also anticipate the cost of goods and services and the levels of compensation paid to employees will increase due to inflationary conditions existing in the general economy. The net losses we incur may fluctuate significantly from quarter to quarter.

We anticipate that our expenses will increase substantially if, and as, we:

- conduct preclinical development activities and initiate investigational new drug, or IND, application-enabling studies and clinical trials in connection with our tau antibody program and our SOD1 ALS gene therapy program;
- continue investing in our gene therapy platform to optimize capsid engineering and payload development, manufacturing, dosing, and delivery techniques by continuing to develop our proprietary antibodies and vectorized antibody platform;
- 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;

- conduct joint research and development under our strategic collaborations for the research, development, and commercialization of certain of our pipeline programs, including our FA Program pursuant to a collaboration with Neurocrine entered into in January 2019, or the 2019 Neurocrine Collaboration Agreement, and our GBA1 gene therapy program pursuant to our collaboration and license agreement with Neurocrine entered into on January 8, 2023, or the 2023 Neurocrine Collaboration Agreement;
- initiate additional preclinical studies and clinical trials for, and continue research and development of, our other 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 that successfully complete clinical development;
- maintain, expand, protect and enforce our intellectual property portfolio;
- identify, acquire or in-license other product candidates and technologies;
- expand our operational, financial and management systems and personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- increase our product liability and clinical trial insurance coverage as we expand our clinical trials and commercialization efforts; and
- continue to operate as a public company.

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

- we are required by the 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 practices, or cGMPs, 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, option, licensing, or other arrangements into which we may enter and performing our obligations in such collaborations;
- obtaining, maintaining, protecting, enforcing and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding and defending against third-party claims of interference or infringement; and
- attracting, hiring and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could

increase beyond expectations if we are required by the FDA, EMA, or other regulatory authorities to redesign or modify preclinical studies or clinical trials or to perform preclinical studies or clinical trials in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate certain of our product development efforts or other operations.

We expect our expenses to increase 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. We also continue to incur 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 December 31, 2022, our cash, cash equivalents, and marketable securities were $118.8 million. Based upon our current operating plan, we expect that our existing cash, cash equivalents, and marketable securities at December 31, 2022, together with the upfront payment received in February 2023 in connection with the 2023 Neurocrine Collaboration Agreement along with amounts expected to be received as reimbursement for development costs under our collaboration and license agreements with Neurocrine, will enable us to meet our planned operating expenses and capital expenditure requirements into 2025.

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 option and license agreements and any similar arrangement we may enter into in the future, including any research and development costs for which we are responsible, and our receipt of any future milestone payments and royalties from our collaboration partners or licensors;
- the extent to which we are obligated to reimburse preclinical development and clinical trial costs, or the achievement of milestones or occurrence of other developments that trigger milestone and royalty payments, under any collaboration or license agreements to which we might become a party, such as our license agreement with Touchlight IP Limited, or Touchlight, which we refer to as the Touchlight License Agreement;
- 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 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 other biological therapy 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 option and license 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 option and license 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 the 2019 Neurocrine Collaboration Agreement and the 2023 Neurocrine 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 option and license 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 option and license arrangements could therefore cause the market price of common stock to decline.

The preclinical stage of our development efforts 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 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 an operating history that included the late stage of clinical development, completion of clinical development, or commercialization of one or more product candidates. All of our active product candidates are currently in preclinical development.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors such as the regulatory setbacks that previously occurred in prior clinical programs we have run including the VY-AADC Program for Parkinson's disease and the VY-HTT01 Program for Huntington's disease, each of which was put on clinical hold by the FDA. These and other events that are part of our operating history 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 other biological therapy 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.

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. Each of the product candidates we are advancing, either alone or together with our strategic collaborators, is currently 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 Hemgenix, an AAV gene therapy

product by CSL Behring LLC for adult patients with Hemophilia B (congenital Factor IX deficiency), 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 Hemgenix, Luxturna, and Zolgensma, as well as Upstaza by PTC, Roctavian by BioMarin Pharmaceuticals, Inc., and 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, EMA, 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. 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.

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 and received feedback from the FDA that, in a disease such as Parkinson's, two adequate and well-controlled clinical trials is suggested.

Any inability to receive timely, actionable feedback from regulatory authorities could also delay or otherwise hinder our development efforts. In October 2020, the FDA notified us that the IND application for our planned Phase 1 and 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 decided in August 2021 not to commence the VYTAL Phase 1 and 2 clinical trial for VY-HTT01 once we had resolved the clinical hold, 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. For example, despite data we believed was promising from the earlier PD-1101 Phase 1b clinical trial and from the separate PD-1102 Phase 1 clinical trial evaluating the delivery of VY-AADC (NBIb-1817), we and our strategic collaborator Neurocrine did not receive favorable data, and were ultimately unable to complete, the RESTORE-1 Phase 2 clinical trial evaluating VY-AADC (NBIb-1817) for the treatment of Parkinson's disease. Similarly, interim results generated from clinical trials do not necessarily predict final results, and results from one completed clinical trial may not be replicated in a subsequent clinical trial with a similar study design. Some of our clinical trials 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.

We are early in our development efforts. All of our active product candidates are currently in preclinical 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 all of our active product candidates are currently 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, among other things, our ability to source animals and other supplies required for the conduct of such testing and studies. If we are unable to obtain such supplies, 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 Cambodia. The supply of these non-human primates is currently constrained due to factors such as their limited worldwide availability, trade relations between the United States and the PRC, and heightened scrutiny of non-human primates originating from Cambodia following allegations in late 2022 that certain Cambodian businesses and government officials may have engaged in the smuggling of non-human primates. 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. In connection with our VY-HTT01 Program for the treatment of Huntington's disease, for example, we were unable to predict what the FDA would require and were unable to obtain a second pre-IND meeting with the FDA to discuss the product candidate's regulatory pathway with the FDA. As a result, in October 2020, the FDA notified us that the IND application for the planned Phase 1 and Phase 2 clinical trial to evaluate VY-HTT01 had been put on clinical hold.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act, known was FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans. Similarly, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

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, for example, we did not initiate the RESTORE-1 Phase 2 clinical trial for VY-AADC (NBIb-1817) as a treatment for Parkinson's disease until we met with OTAT to discuss our proposed trial design and overall development plan. While we 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 BLA, filing or approval.

We also have very limited historical experience with clinical trials. 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;

- 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;
- 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, 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;
- 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 using 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 could cause side effects. 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 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 new drug application or 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 nine 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. 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 even if it is, the FDA determines that it 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 the sameness.

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.

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 and Congress 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 (a) considered a "regenerative medicine therapy" as defined in the Cures Act; (b) intended to treat, modify, reverse, or cure one or more serious or life-threatening diseases or conditions; and (c) 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.

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. We have sought and may in the future seek such a designation for our 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 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. (acquired by Solid Biosciences, Inc., or Solid), Abeona Therapeutics, Inc., Adverum Biotechnologies, Inc., Aevitas Therapeutics, Inc., Akouos, Inc. (acquired by Eli Lilly and Company, or Eli Lilly), Alcyone Therapeutics, Inc., Amicus Therapeutics, Inc., Apic Bio, Inc., Applied Genetic Technologies Corporation (acquired by Syncona Limited), 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), BioMarin, Encoded Therapeutics, Inc., GenSight Biologics SA, Homology Medicines, Inc., LEXEO Therapeutics, Inc., LogicBio Therapeutics, Inc. (acquisition by AstraZeneca announced), 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, REGENXBio Inc., Sarepta Therapeutics, Inc., Solid, 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 discovery platform and preclinical programs will compete with a variety of 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), Freeline Therapeutics Holdings plc, Pfizer, Biogen, Lysogene SA, and Coave Therapeutics SA;

- 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, 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 Tofersen being developed by Biogen, in collaboration with Ionis, and gene therapies being developed by Novartis Gene Therapies, Inc. and Apic Bio, Inc.;

- Our treatment of Freidrich's ataxia under the FA Program will potentially compete with AAV gene therapies being developed by LEXEO Therapeutics, Inc., AavantiBio, Inc. (acquired by Solid), PTC, 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. 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.

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 reply on the reference product, sponsor's data or submit the application as a biosimilar application.

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 ongoing collaborations with Neurocrine, from our ongoing option and license arrangements with Pfizer and Novartis, and from our prior collaborations with Sanofi Genzyme, AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company. If any ongoing or future collaboration or option and license agreements were to be terminated, our business financial condition, results of operations and prospects could be harmed.

To date, all of our revenue has been derived from our ongoing collaborations with Neurocrine, our ongoing option and license arrangements with Pfizer and Novartis, and from our prior collaborations with Sanofi Genzyme and AbbVie. If any ongoing or future collaboration or option and license agreements were to be terminated, our business financial condition, results of operations and prospects could be harmed. For example, certain of our prior collaborations were terminated. As a result of the terminations of our collaborations with Sanofi Genzyme and AbbVie, we ceased to be eligible to receive option and milestone payments pursuant to the collaborations or to receive royalties in connection with any potential products developed under the collaborations.

On February 2, 2021, Neurocrine notified us that it had elected to terminate the 2019 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 2019 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 2019 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 2019 Neurocrine Collaboration Agreement with respect to such programs.

On October 1, 2021, we entered into the Pfizer 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. Effective as of September 30, 2022, Pfizer exercised its option with respect to a capsid in connection with a gene therapy program for the potential treatment of an undisclosed rare neurologic, rare neurological disease, or the Pfizer Option Exercise. Under the terms of the Pfizer Agreement, pursuant to the Pfizer Option exercise, we are eligible to receive specified development, regulatory, and commercialization milestone payments following 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. Pfizer did not exercise its option to license a capsid for a specified cardiovascular disease target under the Pfizer Agreement. As a result, all rights to capsids for that cardiovascular disease target under the Pfizer Agreement have expired and have reverted to us, and we are not eligible to receive any potential future development, regulatory, commercialization, or sales milestone payments or potential royalties pursuant to the Pfizer Agreement in connection with such target.

In March 2022, we entered into the Novartis 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 Agreement, we received an upfront payment of $54.0 million. Effective as of March 1, 2023, Novartis exercised its options to license novel capsids generated from our TRACER capsid discovery platform for use in gene therapy programs against two undisclosed neurologic disease targets. With Novartis' option exercise on two targets, we are entitled to receive a $25.0 million option exercise payment during the first half of 2023, and we are eligible to receive associated potential development, regulatory, and commercial milestone payments, as well as mid- to high-single-digit tiered royalties based on net sales of Novartis products incorporating the licensed capsids. In addition, over the next 18 months, Novartis retains the right to expand the agreement to include options to license capsids for up to two additional rare CNS targets, subject to their availability, for a fee of $18.0 million per target. Under such an expansion, we would be eligible to receive a $12.5 million license option exercise fee for each target exercised, as well as future potential milestone payments per target and mid- to high-single-digit tiered royalties on products incorporating the licensed capsids. Novartis elected not to license a capsid for one CNS target under the Novartis Agreement prior to the expiration of the applicable option period. As a result we are no longer eligible to receive development, regulatory, and commercial milestone payments or royalties in connection with this target, and all capsid rights with respect to that target have returned to us.

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 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, option, licensing, and/or broader collaboration agreements. For example, we entered into the 2023 Neurocrine Collaboration Agreement for the development, manufacture and commercialization of the 2023 Neurocrine

Programs. Our likely collaborators, optionees, 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 option and license transactions on favorable terms or at all. Our ability to generate revenues from our collaborations and option and license transactions will depend on our and our collaborators', optionees', and licensees' abilities to successfully perform the functions assigned to each of us in these arrangements. In addition, our collaborators, optionees, 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, optionee, 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, optionees, or licensees may pose several risks, including the following:

- collaborators, optionees, and licensees have significant discretion in determining the amount and timing of the efforts and resources that they will apply to these collaborations and option and license transactions;

- collaborators, optionees, 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, optionees, 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', optionees', or licensees' strategic focus or available funding or external factors, such as an acquisition, which divert resources or create competing priorities;

- collaborators, optionees, 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, optionees, or licensees could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators, optionees, 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, optionees, 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, optionees, 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 option and license transactions;

- collaborators, optionees, 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 option and license transactions do not result in the successful development and commercialization of products, or if one of our collaborators, optionees, or licensees terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration or option and license 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 our programs relevant to our ongoing collaborations with Neurocrine, 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, optionee, 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 optioned or licensed to it by us. If one of our collaborators, optionees, or licensees terminates its agreement with us, we may find it more difficult to attract new collaborators, optionees, 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, optionees, and licensees.

We will face significant competition in seeking appropriate collaborators, optionees, 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, optionees, and licensees will depend, among other things, upon our assessment of the collaborator's, optionee's, or licensee's resources and expertise, the terms and conditions of the proposed collaboration or option and license transactions and the proposed collaborator's, optionee's, 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, optionee, 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 option and license 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, optionees, 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, optionees, 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 option and license 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 and our collaborators have relied, and we and our collaborators 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 and our collaborators 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 and our collaborators 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 and our collaborators will have agreements governing their activities, we and our collaborators will have limited influence over their actual performance. We and our collaborators will control only certain aspects of our third-party service providers' activities. Nevertheless, we and our collaborators 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 (NBIb-1817) and the separate PD-1102 Phase 1 clinical trial exploring the delivery of VY-AADC (NBIb-1817) using a posterior trajectory were conducted at several locations. Additionally, we had expected to initiate the planned VYTAL Phase 1 and 2 clinical trial for VY-HTT01 at multiple sites in the United States before our decision to refocus the Huntington's disease program. 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 and our collaborators 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 or our collaborators 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 or our collaborators are required to do so due to a service provider's termination of our relationship, then we or our collaborators may be required to source additional technology and personnel in order to perform the relevant activities. We and our collaborators may be unsuccessful in our efforts to internalize some or all relevant activities, either on the desired timeline or at all.

We, our collaborators, 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 and our collaborators 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 and our collaborators 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 flexible manufacturing platform that is based on proprietary technology and provides a scalable process for preclinical and clinical AAV production. We are using HEK 293 cell manufacturing to support our preclinical research activities. We also have expertise with the baculovirus/Sf9 AAV production system, a technology for producing AAV gene therapy vectors at scale in insect-derived cells, which we have used for our clinical development activities in the past and may use in the future for clinical development activities. Both the HEK 293 cell manufacturing process and the baculovirus/Sf9 manufacturing process have been successfully transferred to our contract manufacturing organizations. The baculovirus/Sf9 manufacturing process has also been used by our contract manufacturing organizations in manufacturing clinical materials in accordance with the FDA's cGMPs. If we transition from the use of HEK 293 cell manufacturing for preclinical research activities to the use of the baculovirus/Sf9 AAV production system for clinical development activities, we could encounter transition-related difficulties such as the need to make manufacturing process adjustments, the need to change third-party contract manufacturers, issues with drug potency consistency, and adverse clinical reactions, which could lead us to incur additional costs or delays.

We presently contract with third parties for the manufacturing of our program materials. 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 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.

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 product candidates 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. Our product candidates are in preclinical development. To date, our research and development efforts have focused on our VY-AADC (NBIb-1817) and VY-HTT01 programs. We have terminated our VY-AADC program, and we deprioritized our VY-HTT01 program as we have decided to develop a second-generation product candidate for the treatment of Huntington's disease. Our current portfolio of product candidates is subject to change as we continue to conduct preclinical testing and to develop 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, our assessment of their potential for competitive differentiation, the efficiency of such product candidate's 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, as well as supportive preclinical data. 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. Similar to our prior investments with regard to our VY-AADC (NBIb-1817) and VY-HTT01 program, 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, option and license, 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 and research and development teams, 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.

Recruiting and retaining 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, 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 inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. 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 prices 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 pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, former President Trump issued several executive orders intended to lower the costs of prescription drug products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other

economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, the Department of Health and Human Services, or the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, in November 2020, the HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage of the Inflation Reduction Act has been delayed by Congress to January 1, 2032.

In July 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The order directed the HHS to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." In September 2021, the HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products became the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on any drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay

rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

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 product. 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.

These measures, as well as others adopted in the future, may result in additional downward pressure on the price that we receive for any approved product we or our collaborators might bring to market. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from that we, or our collaborators, may successfully develop and for which we, or they, may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

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, other healthcare providers, 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, and contractual obligations or our 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, costly changes to our business practices, 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 that we may obtain directly or indirectly from health care providers, health plans or other health care industry stakeholders 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 we handle protected health information and whether it 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 certain 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

prescribes 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 went into effect on January 1, 2023 and significantly expanded 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. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The CPRA may apply to some of our business activities. In addition, other states, including Connecticut, Colorado, Utah, and Virginia, have recently passed state privacy laws; Virginia's law became effective January 1, 2023, and the laws in the other three states are scheduled to go into effect later in 2023. 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 require 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. 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 activities occurring in the European Union, which could adversely affect our business, prospects, financial condition and results of operations.

GDPR restrictions on transfers of personal data from the European Union to the United States are unsettled and may impact our business operations. The GDPR generally prohibits transfers of personal data of European Union data subjects outside of the European Union, unless a lawful data transfer solution has been implemented or a specific exception applies. In July 2020, the European Court of Justice invalidated the Privacy Shield program, a voluntary self-certification privacy protection mechanism that facilitated transfers of personal data from the European Union to the United States. The court upheld the validity of an alternative contractual mechanism for such data transfers but required companies to take additional steps, such as evaluating supplementary measures that may need to be taken to protect the transferred personal data. In October 2022, President Biden signed an executive order to implement the European Union -U.S. Data Privacy Framework, which would replace the Privacy Shield. In December 2022, the European Commission began the European Union's process for adopting the European Union-U.S. Data Privacy Framework, but it is unclear if and when the framework will be finalized and whether it will be challenged in court. Continued uncertainty relating to European Union -U.S. data transfers may adversely impact our business operations in the European Union.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. Following the exit of the United Kingdom, or UK, from the European Union, the United Kingdom's 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 clinical trial 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. In addition, if we successfully commercialize any product candidate, we will need to obtain product liability insurance. 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.

Risks Related to the Commercialization of Our Product Candidates

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

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

The use of such data involves risks and uncertainties, and 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 2019 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 2019 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 2019 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, 60% to Neurocrine and 40% to us, 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 2023 Neurocrine Collaboration Agreement, Neurocrine agreed to fund in conducting non-clinical development activities for the GBA1 Program. Upon our receipt of topline data from the first Phase 1 clinical trial for a product candidate being developed pursuant to the GBA1 Program, we will have the option to either: (1) co-commercialize collaboration products in the GBA1 Program 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. In the event the Company exercises its 2023 Co-Co Option, the parties have also agreed that Neurocrine is entitled to receive (in addition to its 50% share of profits) 50% of the Company's share of profits until the Company's obligation to repay 50% of all development costs incurred by Neurocrine in connection with the GBA1 Program prior to such exercise have been paid off out of such 50% of the Company's share of profits. The 2023 Co-Co Trigger Event is the date on which the Company receives topline data from the first Phase 1 clinical trial for a product candidate being developed pursuant to the GBA1 Program.

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 that are selectively engineered, 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, we will be required 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 the use of the licensed intellectual property. For example, The Touchlight License Agreement obligates us to make future milestone and royalty payments if we, or our collaboration partners or TRACER capsid licensees, use a capsid created using certain DNA preparation processes licensed under the Touchlight License 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 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 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 2022 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 licensees 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 licensees 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.

In November 2022, we and Touchlight entered into the Touchlight License Agreement to allow for our historical use of a certain DNA preparation process, or the Subject DNA Preparation Process, and to authorize the prospective exploitation of TRACER capsids that we have previously created using the Subject DNA Preparation Process. As previously referenced in the Risk Factor section of our prior periodic reports, Touchlight had made us aware earlier in 2022 that it believed its intellectual property rights could potentially be asserted against us, although we disagreed with this assessment. In connection with entering into the Touchlight License Agreement, Touchlight also agreed to release any potential claims against us regarding the alleged historical use of certain of Touchlight's intellectual property rights and exploitation of TRACER capsids created with the alleged use of such intellectual property rights.

Potential parties may emerge and 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 licensees 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 regulatory 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.

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 polices may not be consistently maintained. In any such cases, the risk of loss of control or proper management of our proprietary information could jeopardize our intellectual property.

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

Because we currently rely on certain third parties to manufacture all or part of our product candidates and to perform quality testing, and because we collaborate with various organizations and academic institutions for the advancement of our gene therapy 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.

Risks Related to Ownership of Our Common Stock

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 depositary shares, subscription rights, warrants, purchase contract and units, of which we have reserved $75.0 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 8, 2022.

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 January 1, 2022 through December 31, 2022, the sales price of our common stock ranged from a high of $10.60 to a low of $2.60 on the Nasdaq Global Select Market. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased it. The market price for our common stock may be influenced by many factors, including:

- our success in commercializing any product candidates for which we obtain marketing approval;
- regulatory action and results of clinical trials of our product candidates or those of our competitors;
- the success of competitive products or technologies;
- the results of clinical trials of our product candidates;
- the results of clinical trials of product candidates of our competitors;
- the commencement, termination, and success of our collaborations, including the ability or willingness of our collaboration partners to fulfill their obligations to us;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or technologies, the cost of commercializing such product candidates, and the cost of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;

- the ability to secure third-party reimbursement for our product candidates;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- other factors described in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K.

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 (a) a non-affiliate public float in excess of $250 million and annual revenues in excess of $100 million during our last fiscal year, or (b) 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 may cease to qualify as a smaller reporting company as early as June 30, 2023, which would require us to

comply with disclosure requirements that are applicable to other public companies that are not smaller reporting companies following the filing of our Annual Report on Form 10-K for the year ending December 31, 2023, and any portions of our definitive proxy statement relating to our 2024 Annual Meeting of Stockholders incorporated by reference therein. 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.

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 (a) any derivative action or proceeding brought on our behalf, (b) 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, (c) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws or (d) 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

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

As of December 31, 2022, we had both federal and state NOL carryforwards of $175.1 million and $166.5 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Our corporate headquarters are located in Cambridge, Massachusetts. Other operations, including laboratory space, are located in Lexington, Massachusetts. We lease our office and laboratory space, which consist of approximately 26,148 square feet located in Cambridge, Massachusetts and 32,142 square feet located in Lexington, Massachusetts.

ITEM 3. 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 any such matters cannot be predicted with certainty, as of December 31, 2022, we were not party to any material pending proceedings. No material 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 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

Our common stock has been traded on the Nasdaq Global Select Market under the symbol "VYGR" since November 11, 2015. Prior to this time, there was no public market for our common stock.

Stockholders

As of March 1, 2023, there were approximately 12 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have not paid any cash dividends on our common stock since inception and do not anticipate paying cash dividends in the foreseeable future.

Recent Sales of Unregistered Securities

Set forth below is information regarding shares of our common stock issued and stock options granted by us for the twelve months ended December 31, 2022 that were not registered under the Securities Act of 1933, as amended, or the Securities Act and that have not otherwise been described in a Quarterly Report on Form 10-Q or a Current Report on Form 8-K.

On October 1, 2022, we granted to two executives restricted stock unit awards settleable for an aggregate of 163,000 shares of our common stock. On October 17, 2022, we granted stock options to one new employee to purchase

an aggregate of 60,000 shares of our common stock at an exercise price of $6.01 per share. On November 28, 2022, we granted stock options to one new employee to purchase an aggregate of 54,000 shares of our common stock at an exercise price of $5.57 per share. These options and restricted stock units were made outside of our 2015 Stock Option and Incentive Plan as an inducement material to such individual's acceptance of an offer of employment with us in accordance with Nasdaq Listing Rule 5635(c)(4). We intend to file a registration statement on a Form S-8 to register the shares of common stock underlying these inducement awards prior to the time at which the awards become exercisable or settleable, as applicable.

ITEM 6. RESERVED

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth under Item 1A. "Risk Factors" and under "Forward-Looking Statements" in this Annual Report on Form 10-K.

We are a biotechnology company dedicated to breaking through barriers in gene therapy and neurology. We believe the potential of both disciplines has been constrained by delivery challenges; we are leveraging expertise in capsid discovery and neuropharmacology to address these constraints. Our gene therapy platforms enable us to engineer, optimize, manufacture and deliver adeno-associated virus, or 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 other biological therapy 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 an AAV vector or other biological therapy for activity in, efficacy in, or delivery to, the targeted tissue or cells.

We are identifying proprietary AAV capsids, the outer viral protein shells that enclose genetic material that makes up the vector payload. Our team has developed a proprietary AAV capsid discovery platform called TRACER™ (Tropism Redirection of AAV by Cell Type-Specific Expression of RNA) that employs directed evolution to facilitate the selection of AAV capsids with enhanced tissue delivery characteristics, such as more effective delivery across the blood brain barrier, or BBB. 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 that capsids we discover through our TRACER discovery platform, which we refer to as TRACER capsids, have the potential to significantly enhance the efficacy and safety of our single dose gene therapies, which we expect to be delivered with targeted surgical delivery or systemic infusions, as compared with conventional capsids.

In addition to leveraging TRACER capsids in potential licensing arrangements, we are advancing our own proprietary pipeline of drug candidates for neurological diseases. Our wholly-owned prioritized pipeline programs include: superoxide dismutase 1, or SOD1, gene therapy for amyotrophic lateral sclerosis, or ALS, and an anti-tau antibody for Alzheimer's disease. We have identified a lead development candidate for our anti-tau antibody program and we expect to identify a lead development candidate for our SOD1 program during the first half of 2023. We expect to file INDs for both programs in 2024. In addition to these two wholly-owned programs, we are actively advancing two programs in collaboration with Neurocrine Biosciences, Inc., or Neurocrine: a glucocerebrosidase 1, or GBA1, gene therapy program for Parkinson's disease and other GBA1-mediated diseases, and a FXN gene therapy program for Friedreich's ataxia. We also maintain a robust early research pipeline of wholly-owned and collaborative gene therapy programs for neurological diseases.

We have a history of incurring significant losses. We reported a net loss of $46.4 million for the year ended December 31, 2022. As of December 31, 2022, we had an accumulated deficit of $393.5 million. We reported a net loss of $71.2 million for the year ended December 31, 2021. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially in connection with our ongoing activities, as we:

- conduct preclinical development activities and initiate investigational new drug, or IND, application-enabling studies and clinical trials in connection with our tau antibody program and our SOD1 ALS gene therapy program;
- continue investing in our gene therapy platform to optimize capsid engineering and payload development, manufacturing, dosing, and delivery techniques by continuing to develop our proprietary antibodies and vectorized antibody platform;
- increase our investment in and support for TRACERTM (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;
- conduct joint research and development under our strategic collaborations for the research, development, and commercialization of certain of our pipeline programs, including our FA Program pursuant to a collaboration with Neurocrine entered into in January 2019, or the 2019 Neurocrine Collaboration Agreement, and our GBA1 gene therapy program pursuant to our collaboration and license agreement with Neurocrine entered into on January 8, 2023, or the 2023 Neurocrine Collaboration Agreement;
- initiate additional preclinical studies and clinical trials for, and continue research and development of, our other 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 that successfully complete clinical development;
- maintain, expand, protect and enforce our intellectual property portfolio;
- identify, acquire or in-license other product candidates and technologies;
- expand our operational, financial and management systems and personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- increase our product liability and clinical trial insurance coverage as we expand our clinical trials and commercialization efforts; and
- continue to operate as a public company.

We refer to our collaboration agreement with Neurocrine dated as of January 28, 2019 as the 2019 Neurocrine Collaboration Agreement. We refer to our option and license agreement with Pfizer Inc., or Pfizer, as the Pfizer Agreement, and to our option and license agreement with Novartis Pharma AG, or Novartis, as the Novartis Agreement.

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 year ended December 31, 2022, we recognized $40.9 million of collaboration revenue from the Pfizer Agreement and the 2019 Neurocrine Collaboration Agreement. For additional information about our revenue recognition policy, see the section titled "—Critical Accounting Policies and Estimates—Revenue."

For the foreseeable future, we expect substantially all of our revenue will be generated from the 2019 Neurocrine Collaboration Agreement and the 2023 Neurocrine Collaboration Agreement, the Pfizer Agreement, the Novartis Agreement, and any other strategic collaborations and out-licensing arrangements we may enter into in the future. If our development efforts are successful, we may also generate revenue from product sales.

Expenses

Research and Development Expenses

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

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- costs of funding research performed by third parties that conduct research and development, preclinical activities, manufacturing and production design on our behalf;
- the cost of purchasing laboratory supplies and non-capital equipment used in designing, developing and manufacturing preclinical study materials;
- consultant fees;
- facility costs including rent, depreciation and maintenance expenses;
- the cost of securing and protecting intellectual property rights associated with our research and development activities; 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.

Research and development activities are central to our business model. We are in the early stages of development of our product candidates. On August 6, 2021, our board of directors approved a strategic restructuring plan to eliminate a portion of our workforce as part of an initiative to reduce expenses and enhance operations. Our research and development costs have decreased relative to pre-2021 levels as a result of this strategic restructuring, and also due to 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. However, 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.

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. Our expenses will increase if:

- we are required by the 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.

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. 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, Net

Other income, net consists primarily of an employee retention tax credit under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, and interest income on our marketable securities.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our consolidated financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the financial statements prospectively from the date of change in estimates.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies used in the preparation of our financial statements require the most significant judgments and estimates.

Revenue Recognition – ASC 606

We recognize revenue in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 606 *Revenue from Contracts with Customers,* or ASC 606.

We enter into license, option, and collaboration agreements which are within the scope of ASC 606, under which we license or provide options to license certain of our product candidates and, in certain cases, perform research and development. The terms of these arrangements typically include payment of one or more of the following: non-

refundable, upfront fees; reimbursement of research and development costs; development, regulatory and commercial milestone payments; option exercise fees; and royalties on net sales of licensed products.

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

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

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

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

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

Upfront payments and fees are recorded as contract liabilities within deferred revenue upon receipt or when due until we perform our obligations under these arrangements. Amounts are recorded as accounts receivable when our rights to consideration are unconditional. A significant portion of revenue recognized from the 2019 Neurocrine Collaboration Agreement is related to performance obligations pursuant to which revenue is recognized using a proportional performance model. Revenue is recognized using input-based measurements, which involves the measurement of progress toward each performance obligation based on the actual costs incurred compared to total projected costs. We estimate the expected remaining costs to complete the research and development services for each performance obligation. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure and related

revenue recognition. Changes in our estimates of the expected remaining costs to complete the research and development services for our performance obligations, such as the significant change that occurred in the fourth quarter of 2021 as a result of decisions made by the JSC for the 2019 Neurocrine Collaboration Agreement, can result in significant changes to the amount of revenue we recognize each period.

Results of Operations

Comparison of the years ended December 31, 2022 and 2021:

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021, respectively, together with the changes in those items in dollars:

	Year ended December 31,		
	2022	2021	Change
		(in thousands)	
Collaboration revenue	$ 40,907	$ 37,415	$ 3,492
Operating expenses:			
Research and development	60,764	73,787	(13,023)
General and administrative	30,980	37,246	(6,266)
Total operating expenses	91,744	111,033	(19,289)
Other income, net:			
Interest income (expense)	1,792	(390)	2,182
Other income	2,653	2,811	(158)
Total other income, net	4,445	2,421	2,024
Loss before income taxes	(46,392)	(71,197)	24,805
Income tax provision	16	—	16
Net loss	$ (46,408)	$ (71,197)	$ 24,789

Collaboration Revenue

Collaboration revenue was $40.9 million for the year ended December 31, 2022, and $37.4 million for the year ended December 31, 2021. The increase in collaboration revenue was largely a result of revenue recognized in connection with Pfizer's decision to exercise the first material right for the option to receive an exclusive license, or the Pfizer License Option, along with the expiration of the second material right associated with the Pfizer License Option. This resulted in total revenue recognized of $40.0 million from Pfizer during the year ended December 31, 2022. The increase in collaboration revenue is partially offset by decreased revenue recognized under the 2019 Neurocrine Collaboration Agreement during the year ended December 31, 2022. During the fourth quarter of 2021, we recorded significant revenue associated with a change in estimate of the expected remaining costs to complete the research and development services for our performance obligations under the 2019 Neurocrine Collaboration Agreement, resulting in a significant decrease in revenue to be recorded in future periods. During the year ended December 31, 2021, collaboration revenue was entirely related to research services and cost reimbursement from the 2019 Neurocrine Collaboration Agreement. Our collaboration revenues were not materially impacted by the COVID-19 pandemic during the year ended December 31, 2022.

Research and Development Expense

Research and development expense decreased by $13.0 million from $73.8 million for the year ended December 31, 2021 to $60.8 million for the year ended December 31, 2022. The following table summarizes our research and development expenses for the years ended December 31, 2022 and 2021:

	Year ended December 31,		
	2022	2021	Change
	(in thousands)		
Employee and consultant	$ 29,209	$ 36,385	$ (7,176)
External research and development	15,679	18,486	(2,807)
Facilities and other	7,863	9,483	(1,620)
Professional fees	8,014	9,433	(1,420)
Total research and development expenses	$ 60,764	$ 73,787	$ (13,023)

The decrease in research and development expense for the year ended December 31, 2022 was primarily attributable to the following:

- approximately $7.2 million for decreased compensation costs and stock-based compensation costs associated with lower headcount in research and development functions compared to prior year;
- approximately $2.8 million for decreased 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 Huntington's disease and a reduction in external costs incurred in connection with the 2019 Neurocrine Collaboration Agreement, partially offset by the technology access fee for our license agreement with Touchlight IP Limited, or the Touchlight License Agreement;
- approximately $1.6 million of decreased facility costs primarily related to the termination of the lease for office and laboratory space at 75 Sidney Street during the second quarter of 2022; and
- approximately $1.4 million for decreased professional fees and related expenses to support the pipeline programs.

General and Administrative Expense

General and administrative expense decreased by $6.3 million from $37.2 million for the year ended December 31, 2021 to $31.0 million for the year ended December 31, 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 costs associated with lower headcount in general and administrative functions as compared to prior year;
- approximately $1.6 million for decreased facility and other costs primarily related to the termination of the lease for office and laboratory space at 75 Sidney Street during the second quarter of 2022; and
- approximately $1.5 million for decreased legal costs and intellectual property related expenses.

Other Income, Net

Other income, net of approximately $4.4 million was recognized during the year ended December 31, 2022, as compared to $2.4 million during the year ended 2021. Other income, net during the year ended December 31, 2022 primarily related to an employee retention tax credit under the CARES Act and interest income on marketable securities

balances, while other income, net during the year ended December 31, 2021 primarily related to interest income on marketable securities balances.

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, strategic collaborations and option and license arrangements, including our 2019 Neurocrine Agreement and 2023 Neurocrine Collaboration Agreement, our ongoing option and license arrangements with Pfizer and Novartis under the Pfizer Agreement and the Novartis Agreement, respectively, and with our prior collaboration agreements.

As of December 31, 2022, we had cash, cash equivalents, and marketable securities of $118.8 million. Based upon our current operating plan, we expect that our existing cash, cash equivalents, and marketable securities at December 31, 2022, together with the upfront payment received in February 2023 in connection with the 2023 Neurocrine Collaboration Agreement, along with amounts expected to be received as reimbursement for development costs under our 2019 Neurocrine Agreement and 2023 Neurocrine Collaboration Agreement, will enable us to meet our planned operating expenses and capital expenditure requirements into 2025.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2022, 2021, and 2020.

	Year ended December 31,		
	2022	2021	2020
	(in thousands)		
Net cash (used in) provided by:			
Operating activities	$ (12,509)	$ (53,525)	$ (96,716)
Investing activities	(7,339)	65,906	112,995
Financing activities	1,110	612	3,163
Net (decrease) increase in cash, cash equivalents, and restricted cash	$ (18,738)	$ 12,993	$ 19,442

Cash Flows from Operating Activities

Net cash used in operating activities was $12.5 million during the year ended December 31, 2022. The cash used in operating activities for the year ended December 31, 2022 was primarily driven by operating expenses, net of stock-based compensation and depreciation, offset by an increase in deferred revenue partially driven by the upfront payment of $54.0 million from Novartis during the year ended December 31, 2022.

Net cash used in operating activities was $53.5 million during the year ended December 31, 2021. The cash used in operating activities for the year ended December 31, 2021 was primarily driven by operating expenses, net of stock-based compensation and depreciation. We also received an upfront payment of $30.0 million pursuant to the Pfizer Agreement.

Net cash used in operating activities was $96.7 million during the year ended December 31, 2020. The cash used in operating activities for the year ended December 31, 2020 was primarily driven by the one-time recognition of $105.2 million deferred revenue related to the termination of the AbbVie Tau Collaboration and the AbbVie Alpha-Synuclein Collaboration, offset by $36.7 million of net income, and changes in working capital.

Cash Flows from Investing Activities

Net cash used in investing activities was $7.3 million during the year ended December 31, 2022. The cash used in investing activities for the year ended December 31, 2022 was primarily due to $54.8 million for purchases of marketable securities and $2.5 million for purchases of property and equipment, offset by $50.0 million from proceeds from maturities and sales of marketable securities.

Net cash provided by investing activities was $65.9 million during the year ended December 31, 2021. The cash provided by investing activities for the year ended December 31, 2021 was primarily due to $70.0 million from maturities of marketable securities and $12.6 million from proceeds of sales of marketable securities partially offset by $15.1 million for purchases of marketable securities and $1.6 million for purchases of property and equipment.

Net cash provided by investing activities was $113.0 million during the year ended December 31, 2020. The cash provided by investing activities for the year ended December 31, 2020 was primarily due to proceeds from maturities of marketable securities of $195.5 million, offset by purchases of marketable securities of $70.4 million and purchases of property and equipment of $12.1 million.

Cash Flows from Financing Activities

Net cash provided by financing activities was $1.1 million during the year ended December 31, 2022 primarily due to the proceeds from the exercise of stock options, and purchases by our employees of our common stock under our employee stock purchase plan.

Net cash provided by financing activities was $0.6 million during the year ended December 31, 2021 primarily due to the proceeds from the exercise of stock options, and purchases by our employees of our common stock under our employee stock purchase plan.

Net cash provided by financing activities was $3.2 million during the year ended December 31, 2020 primarily due to the proceeds from the exercise of stock options, and purchases by our employees of our common stock under our employee stock purchase plan.

Funding Requirements

Our expenses decreased during the year ended December 31, 2022 as compared with the prior year 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 longer term, 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, executing financial statement controls, satisfying regulatory and quality standards, fulfilling healthcare compliance requirements, and maintaining product, clinical trial and directors' and officers' liability insurance coverage. We also anticipate the cost of goods and services and the levels of compensation paid to employee will increase due to inflationary conditions existing in the general economy. 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 December 31, 2022, together with the upfront payment received in February 2023 in connection with the 2023 Neurocrine Collaboration Agreement, along with amounts expected to be received as reimbursement for development costs under our 2019 Neurocrine Agreement and 2023 Neurocrine Collaboration Agreement, will enable us

to meet our planned operating expenses and capital expenditure requirements into 2025. 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 option and license agreements and any similar arrangement we may enter into in the future, including any research and development costs for which we are responsible, and our receipt of any future milestone payments and royalties from our collaboration partners or licensors;
- the extent to which we are obligated to reimburse preclinical development and clinical trial costs, or the achievement of milestones or occurrence of other developments that trigger milestone and royalty payments, under any collaboration or license agreements to which we might become a party, such as the Touchlight License Agreement;
- 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 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 option and license 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 option and license 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 option and license 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 generally are 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. In certain instances, we are also obligated to pay our licensors royalties based on sales of products, if approved, using the intellectual property licensed under 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. For more information, refer to Note 7 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

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 rules of the Securities and Exchange Commission, or the SEC.

Smaller Reporting Company Status

As of June 30, 2022, we have requalified as 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 (a) a non-affiliate public float in excess of $250 million and annual revenues in excess of $100 million during our last fiscal year, or (b) 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 may cease to qualify as a smaller reporting company as early as June 30, 2023, which would require us to comply with disclosure requirements that are applicable to other public companies that are not smaller reporting companies following the filing of our Annual Report on Form 10-K for the year ending December 31, 2023, and any portions of our definitive proxy statement relating to our 2024 Annual Meeting of Stockholders incorporated by reference therein.

ITEM 7A. 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, we believe 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 costs of labor, goods, and services. We do not believe that inflation had, or that an immediate 100 basis point change in inflation would have had, a material effect on our business, financial condition, or results of operations during the year ended December 31, 2022.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Management's Evaluation of Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(c) 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 December 31, 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 December 31, 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.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company's principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company's board of directors, management, and other personnel, 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 and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of a company's assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that a company's receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision of and with the participation of our principal executive officer and principal financial and accounting officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control—Integrated Framework (2013 framework). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during our fiscal quarter ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

Not applicable.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Incorporated by reference from the information in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

ITEM 11. EXECUTIVE COMPENSATION

Incorporated by reference from the information in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Incorporated by reference from the information in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

Incorporated by reference from the information in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Incorporated by reference from the information in our Proxy Statement for our 2023 Annual Meeting of Stockholders, which we expect to file with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a)(1) Financial Statements.

(a)(2) Financial Statement Schedules.

All schedules have been omitted because they are not required or because the required information is given in the Consolidated Financial Statements or Notes thereto set forth under Item 8 above.

(a)(3) Exhibits.

See the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The exhibits listed in the Exhibit Index below are filed or incorporated by reference as part of this Annual Report on Form 10-K.

ITEM 16. FORM 10-K SUMMARY

This Annual Report on Form 10-K does not include a summary.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Voyager Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Voyager Therapeutics, Inc. (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive (loss) income, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Revenue recognition under the proportional performance model

Description of the Matter	As discussed in Note 9 to the consolidated financial statements, in 2019 the Company entered into a Collaboration Agreement which resulted in collaboration revenue of $0.9 million for the year ended December 31, 2022 and deferred revenue of $11.8 million as of December 31, 2022. The Company recognizes consideration allocated to each performance obligation using the proportional performance method. Revenue is recognized using input-based measurements, which involves the measurement of progress toward each performance obligation based on the actual costs incurred compared to total projected costs.

Auditing collaboration revenue recognized was especially challenging and judgmental because the proportional performance calculation involves subjective management assumptions about estimates of the expected remaining costs to complete the research and development services for each performance obligation. Changes in expected remaining costs to complete can have a material effect on the amount of collaboration revenue recognized.

How We Addressed the Matter in Our Audit

Our audit procedures included, among others, the inspection of the Company's contract and testing of the completeness and accuracy of the underlying data used to determine the expected remaining costs to complete the research and development services for each performance obligation. We performed inquiries of research and development personnel to validate management's estimates and obtained corroborative evidence to assess the reasonableness of the proportional performance calculation. We also performed a retrospective review to assess the Company's historical estimates of the remaining costs to complete the research and development services and a sensitivity analysis to evaluate the materiality of reasonable changes in management's assumptions.

/s/ *Ernst & Young LLP*

We have served as the Company's auditor since 2015.

Boston, Massachusetts
March 7, 2023

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

	December 31,	
	2022	**2021**
Assets		
Current assets:		
Cash and cash equivalents	$ 98,959	$ 117,433
Marketable securities	19,889	15,106
Related party collaboration receivable	257	732
Prepaid expenses and other current assets	5,394	3,427
Total current assets	124,499	136,698
Property and equipment, net	17,857	21,920
Deposits and other non-current assets	1,515	1,779
Operating lease, right-of-use assets	15,485	33,458
Total assets	$ 159,356	$ 193,855
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,566	$ 574
Accrued expenses	7,816	10,950
Other current liabilities	2,832	5,571
Deferred revenue, current	59,377	33,886
Total current liabilities	72,591	50,981
Deferred revenue, non-current	6,450	8,210
Other non-current liabilities	21,295	39,609
Total liabilities	100,336	98,800
Commitments and contingencies (see note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value: 5,000,000 shares authorized; no shares issued and outstanding at December 31, 2022 and 2021	—	—
Common stock, $0.001 par value: 120,000,000 shares authorized; 38,613,891 and 37,918,395 shares issued and outstanding at December 31, 2022 and 2021, respectively	38	38
Additional paid-in capital	452,713	442,259
Accumulated other comprehensive loss	(219)	(138)
Accumulated deficit	(393,512)	(347,104)
Total stockholders' equity	59,020	95,055
Total liabilities and stockholders' equity	$ 159,356	$ 193,855

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

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

	Year ended December 31,		
	2022	**2021**	**2020**
Collaboration revenue	$ 40,907	$ 37,415	$ 171,128
Operating expenses:			
Research and development	60,764	73,787	108,753
General and administrative	30,980	37,246	34,991
Total operating expenses	91,744	111,033	143,744
Operating (loss) income	(50,837)	(73,618)	27,384
Other income, net:			
Interest income (expense)	1,792	(390)	1,659
Other income	2,653	2,811	7,698
Total other income, net	4,445	2,421	9,357
(Loss) income before income taxes	(46,392)	(71,197)	36,741
Income tax provision	16	—	—
Net (loss) income	$ (46,408)	$ (71,197)	$ 36,741
Other comprehensive (loss) income			
Net unrealized loss on available-for-sale-securities	(81)	(4)	(30)
Total other comprehensive loss	(81)	(4)	(30)
Comprehensive (loss) income	$ (46,489)	$ (71,201)	$ 36,711
Net (loss) income per share, basic	$ (1.21)	$ (1.89)	$ 0.99
Net (loss) income per share, diluted	(1.21)	(1.89)	$ 0.98
Weighted-average common shares outstanding, basic	38,356,810	37,668,947	37,132,447
Weighted-average common shares outstanding, diluted	38,356,810	37,668,947	37,348,514

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

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

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Stockholders'
	Shares	Amount	Capital	Loss	Deficit	Equity
Balance at December 31, 2019	36,865,116	$ 37	$ 412,227	$ (104)	$ (312,648)	$ 99,512
Exercises of vested stock options	228,436	—	2,319	—	—	2,319
Vesting of restricted stock units	170,367	—	—	—	—	—
Issuance of common stock under ESPP	104,108	—	1,279	—	—	1,279
Stock-based compensation expense	—	—	14,499	—	—	14,499
Unrealized loss on available-for-sale securities	—	—	—	(30)	—	(30)
Net income	—	—	—	—	36,741	36,741
Balance at December 31, 2020	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	346,551	—	—	—	—	—
Issuance of common stock under ESPP	200,006	—	918	—	—	918
Stock-based compensation expense	—	—	10,990	—	—	10,990
Unrealized loss on available-for-sale securities	—	—	—	(4)	—	(4)
Net loss	—	—	—	—	(71,197)	(71,197)
Balance at December 31, 2021	37,918,395	$ 38	$ 442,259	$ (138)	$ (347,104)	$ 95,055
Exercises of vested stock options	89,012	—	629	—	—	629
Vesting of restricted stock units	456,219	—	—	—	—	—
Issuance of common stock under ESPP	150,265	—	672	—	—	672
Stock-based compensation expense	—	—	9,153	—	—	9,153
Unrealized loss on available-for-sale securities	—	—	—	(81)	—	(81)
Net loss	—	—	—	—	(46,408)	(46,408)
Balance at December 31, 2022	38,613,891	$ 38	$ 452,713	$ (219)	$ (393,512)	$ 59,020

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

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

	Year ended December 31,		
	2022	**2021**	**2020**
Cash flow from operating activities			
Net (loss) income	$ (46,408)	$ (71,197)	$ 36,741
Adjustments to reconcile net (loss) income to net cash used in operating activities:			
Stock-based compensation expense	9,344	11,324	14,934
Depreciation	6,191	5,165	3,817
Amortization of premiums and discounts on marketable securities	(16)	349	27
Gain on Lease Termination	(2,468)	—	—
Change in fair value of common stock and warrants to purchase equity securities	—	(2,460)	(7,698)
Loss on disposal of fixed assets	377	—	—
Changes in operating assets and liabilities:			
Related party collaboration receivable	475	7,280	10,484
Prepaid expenses and other assets	(1,967)	1,883	(551)
Operating lease, right-of-use assets	3,462	2,606	(7,592)
Other non-current assets	(152)	69	275
Accounts payable	1,992	(60)	(3,436)
Accrued expenses	(3,148)	(3,335)	(6,480)
Operating lease liabilities	(3,922)	(3,428)	13,439
Deferred revenue	23,731	(1,721)	(150,676)
Net cash used in operating activities	(12,509)	(53,525)	(96,716)
Cash flow from investing activities			
Purchases of property and equipment	(2,491)	(1,609)	(12,097)
Purchases of marketable securities	(54,848)	(15,117)	(70,403)
Proceeds from sales and maturities of marketable securities	50,000	82,632	195,495
Net cash (used in) provided by investing activities	(7,339)	65,906	112,995
Cash flow from financing activities			
Proceeds from the exercise of stock options	629	28	2,319
Proceeds from the purchase of common stock under ESPP	481	584	844
Net cash provided by financing activities	1,110	612	3,163
Net (decrease) increase in cash and cash equivalents	(18,738)	12,993	19,442
Cash, cash equivalents, and restricted cash beginning of period	119,212	106,219	86,777
Cash, cash equivalents, and restricted cash end of period	$ 100,474	$ 119,212	$ 106,219
Supplemental disclosure of cash and non-cash activities			
Operating lease right-of-use assets obtained in exchange for operating lease liabilities	$ —	$ 664	$ 10,818
Capital expenditures incurred but not yet paid	$ 14	$ 80	$ 831

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

1. Nature of business

Voyager Therapeutics, Inc. (the "Company") is a biotechnology company dedicated to breaking through barriers in gene therapy and neurology. The Company focuses on leveraging its expertise in capsid discovery and neuropharmacology to address the delivery hurdles that have constrained the gene therapy and neurology disciplines, with the goal of either halting or slowing 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 adeno-associated virus ("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 other biological therapy 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 an AAV vector or other biological therapy for activity in, efficacy in, or delivery to, the targeted tissue or cells.

The Company is identifying proprietary AAV capsids, the outer viral protein shells that enclose genetic material that makes up the vector 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) that employs directed evolution to facilitate the selection of AAV capsids with enhanced tissue delivery characteristics, such as more effective delivery across the blood brain barrier ("BBB"). 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 that the capsids it discovers through its TRACER discovery platform ("TRACER Capsids") have the potential to significantly enhance the efficacy and safety of its single dose gene therapies, which it expects to be delivered with targeted surgical delivery or systemic infusions, as compared with conventional capsids.

The Company has a history of incurring annual net operating losses. As of December 31, 2022, the Company had an accumulated deficit of $393.5 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 collaborations with Neurocrine Biosciences, Inc. ("Neurocrine"), its option and license agreement with Pfizer, Inc. ("Pfizer"), and its option and license agreement with Novartis Pharma AG ("Novartis").

As of December 31, 2022, the Company had cash, cash equivalents, and marketable securities of $118.8 million. Based upon its current operating plan, the Company expects that its existing cash, cash equivalents, and marketable securities at December 31, 2022, together with the upfront payment received in February 2023 in connection with the Collaboration and License Agreement by and between the Company and Neurocrine dated as of January 8, 2023 (the "2023 Neurocrine Collaboration Agreement"), along with amounts expected to be received as reimbursement for development costs under the Company's collaboration and license agreements with Neurocrine, will be sufficient to meet the Company's planned operating expenses and capital expenditure requirements into 2025.

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 consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP") and pursuant to the rules and regulations of the U.S. Securities and Exchange Commission ("SEC") for reporting on Form 10-K. The Company's consolidated financial statements include the accounts of Voyager Therapeutics, Inc. and its wholly-owned subsidiary, Voyager Securities Corporation. All intercompany balances 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.

Fair Value of Financial Instruments

ASC Topic 820, *Fair Value Measurement* ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- *Level 1*—Quoted market prices in active markets for identical assets or liabilities.
- *Level 2*—Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates, and yield curves.
- *Level 3*—Unobservable inputs developed using estimates of assumptions developed by the Company, which reflect those that a market participant would use.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values, due to their short-term nature.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in money market funds.

Marketable Securities

The Company classifies marketable securities with a remaining maturity of greater than three months when purchased as available-for-sale. Marketable securities with a remaining maturity date greater than one year and marketable equity securities are classified as non-current where the Company has the intent and ability to hold these securities for at least the next 12 months.

All available for sale debt securities are carried at fair value with the unrealized gains and losses included in other comprehensive (loss) income as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense. Realized gains and losses are determined using the specific identification method and are included in other income. If any adjustment to fair value reflects a decline in value of the investment, the Company uses a forward-looking approach based on expected losses to estimate credit losses on certain types of financial instruments, including trade receivables and available-for-sale debt securities. No other than temporary losses have been recognized.

Cash, cash equivalents, and marketable securities as of December 31, 2022 and 2021 consist of the following:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
		(in thousands)		
As of December 31, 2022				
Money market funds included in cash and cash equivalents	$ 91,724	—	—	$ 91,724
Marketable securities- U.S. Treasury notes	19,980	—	(91)	19,889
Total money market funds and marketable securities	$ 111,704	$ —	$ (91)	$ 111,613
As of December 31, 2021				
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	$ 115,422	$ —	$ (11)	$ 115,411

All of the Company's marketable securities at December 31, 2022 and 2021 have a contractual maturity of one year or less.

Restricted Cash

As of December 31, 2022 and 2021, the Company maintained restricted cash totaling approximately $1.5 million and $1.8 million, respectively, held in the form of money market accounts as collateral for the Company's facility lease obligations. The balance is included within deposits and other non-current assets in the accompanying consolidated balance sheets. The following table provides a reconciliation of cash, cash equivalents, and restricted cash within the consolidated balance sheets that sum to the total of the same such amounts shown in the statements of cash flows:

	As of December 31,		
	2022	2021	2020
		(in thousands)	
Cash and cash equivalents	$ 98,959	$ 117,433	$ 104,440
Restricted cash included in deposits and other non-current assets	1,515	1,779	1,779
Total cash, cash equivalents, and restricted cash	$ 100,474	$ 119,212	$ 106,219

Property and Equipment

Property and equipment consists of laboratory equipment, furniture and office equipment, and leasehold improvements and is stated at cost, less accumulated depreciation. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred; while costs of major additions and

betterments are capitalized. Depreciation is calculated over the estimated useful lives of the assets using the straight-line method.

Impairment of Long-Lived Assets

The Company evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company has not recognized any impairment losses from inception through December 31, 2022.

Revenue Recognition

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

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

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

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

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

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

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

Upfront payments and fees are recorded as contract liabilities within deferred revenue on the consolidated balance sheets until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional. A significant portion of revenue recognized from the 2019 Neurocrine Collaboration Agreement is related to performance obligations pursuant to which revenue is recognized using a proportional performance model. Revenue is recognized using input-based measurements, which involves the measurement of progress toward each performance obligation based on the actual costs incurred compared to total projected costs. The Company estimates the expected remaining costs to complete the research and development services for each performance obligation. The Company evaluates the measure of progress each reporting period and, if necessary, adjust the measure and related revenue recognition.

Research and Development

Research and development costs are charged to expense as incurred in performing research and development activities. The costs include employee compensation costs, external research, consultant costs, sponsored research, license fees, process development and facilities costs. Facilities costs primarily include the allocation of rent, utilities and depreciation.

Leases

The Company determines if an arrangement is or contains a lease at inception under Accounting Standards Codification (ASC) 842 *Leases*. For leases with a term of 12 months or less, the Company does not recognize a right-of-use asset or lease liability. The Company's operating leases are recognized on its consolidated balance sheet as operating lease, right-of-use asset, other current liabilities, and other non-current liabilities. The Company does not have any finance leases.

Right-of-use assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease right-of-use assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. As the Company's leases typically do not provide an implicit rate, the Company uses an estimate of its incremental borrowing rate based on the information available at the lease commencement date in determining the

present value of lease payments. Operating lease right-of-use assets also include the effect of any lease prepaid or deferred lease payments and are reduced by lease incentives. The lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Lease expense is recognized on a straight-line basis over the lease term.

The Company has lease agreements with lease and non-lease components, which are generally accounted for separately. Non-lease components as it pertains to the Company's leased premises generally refer to common area maintenance charges related to the premises.

Research Contract Costs and Accruals

The Company has entered into various research and development contracts with research institutions and other companies. These agreements are generally cancelable. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

The Company expenses patent application and related legal costs as incurred and classifies such costs as general and administrative expenses in the accompanying statements of operations.

Stock-Based Compensation Expense

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718 *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees, directors, and other service providers, referred to as non-employees, including grants of restricted stock units and stock options, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. The Company estimates the fair value of options granted using the Black-Scholes option pricing model. The Company uses the fair value of its common stock to determine the fair value of restricted stock awards and restricted stock units.

The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the expected term of the award, (c) the risk-free interest rate and (d) expected dividends. The Company bases the estimate of expected volatility on the historical volatility of its common stock. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for stock options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. For stock options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

The Company expenses the fair value of its stock-based compensation awards on a straight-line basis over the associated service period, which is generally the period in which the related services are received, adjusted for actual forfeitures of unvested awards as they occur.

The Company records the expense for stock-based compensation awards subject to performance conditions over the remaining service period when management determines that achievement of the performance condition is probable. Management evaluates when the achievement of a performance condition is probable based on the expected satisfaction of the performance conditions as of the reporting date.

Income Taxes

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and the tax reporting basis of assets and liabilities and are measured using the enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the weight of available evidence, it is more likely than not that the deferred tax assets will be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2022, the Company does not have any significant uncertain tax positions.

Comprehensive (Loss) Income

Comprehensive (loss) income is comprised of net (loss) income and other comprehensive income or loss. Other comprehensive income or loss consists of unrealized gains or losses on marketable securities.

Net (Loss) Income Per Share

Basic net (loss) income per share is calculated by dividing the net (loss) income by the weighted-average number of shares of common stock outstanding during the period, without consideration for potentially dilutive securities. Diluted net (loss) income per share is computed by dividing the net (loss) income by the weighted-average number of shares of common stock and potentially dilutive securities outstanding for the period determined using the treasury-stock and if-converted methods.

For purposes of the diluted net (loss) income per share, unvested restricted common stock and outstanding stock options are considered to be potentially dilutive securities. Unvested restricted common stock and outstanding stock options were excluded from the calculation of diluted net loss per share in the years ended December 31, 2022 and 2021, because their effect would be anti-dilutive and therefore, basic and diluted net loss per share were the same for the years ended December 31, 2022 and 2021.

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

	As of December 31,		
	2022	2021	2020
Unvested restricted common stock awards	45,000	137,255	156,863
Unvested restricted common stock units	1,112,563	806,379	527,625
Outstanding stock options	6,199,571	5,013,193	5,379,856
Total	7,357,134	5,956,827	6,064,344

Basic net (loss) income and diluted weighted-average shares outstanding are as follows for the years ended December 31, 2022, 2021, and 2020:

	Year Ended December 31,		
	2022	2021	2020
	(in thousands, except share data)		
Numerator:			
Net (loss) income	$ (46,408)	$ (71,197)	$ 36,741
Denominator for basic net (loss) income per share:			
Weighted average shares outstanding-basic	38,356,810	37,668,947	37,132,447
Denominator for diluted net (loss) income per share:			
Weighted average shares outstanding	38,356,810	37,668,947	37,132,447
Common stock options and restricted stock units	—	—	216,068
Weighted average shares outstanding-diluted	38,356,810	37,668,947	37,348,514

Concentrations of Credit Risk and Significant Suppliers

The Company has no financial instruments with off-balance sheet risk such as foreign exchange contracts, option contracts or other foreign currency hedging arrangements. Financial instruments that potentially subject the Company to a concentration of credit risk are cash and cash equivalents. The Company's cash is held in accounts at financial institutions that may exceed federally insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds.

The Company is dependent on third-party manufacturers to supply certain products for research and development activities in its programs. In particular, the Company relies on a sole manufacturer to supply it with specific vectors related to the Company's research and development programs.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker in deciding how to allocate resources and assess performance. The Company and the Company's chief operating decision maker, the Company's Chief Executive Officer, view the Company's operations and manages its business as a single operating segment, which is the business of developing and commercializing gene therapies.

Recent Accounting Pronouncements

In August 2020, the FASB issued ASU No. 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40)*. This standard amends the guidance on convertible instruments and the derivatives scope exception for contracts in an entity's own equity and amends the related earnings per share ("EPS") guidance. The ASU will be effective for smaller reporting companies for fiscal years beginning after December 15, 2023 and interim periods within those fiscal years. Early adoption is permitted in fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The Company is assessing the impact of ASU 2020-06 on the consolidated financial statements and does not expect it to have a material impact.

3. Fair value measurements

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

Assets	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)		
December 31, 2022				
Money market funds included in cash and cash equivalents	$ 91,724	$ 91,724	$ —	$ —
Marketable securities- U.S. Treasury notes	19,889	19,889	—	—
Total	$ 111,613	$ 111,613	$ —	$ —
December 31, 2021				
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. Treasuries based on quoted prices in active markets for identical securities.

4. Prepaid expenses and other current assets

Prepaid expenses and other current assets consist of the following:

	As of December 31, 2022	2021
	(in thousands)	
Other current assets	$ 4,233	$ 1,701
Prepaid insurance	696	1,360
Prepaid research and development contracts	83	350
Accrued interest receivable	382	16
Total	$ 5,394	$ 3,427

5. Property and equipment, net

Property and equipment, net consists of the following:

	As of December 31, 2022	2021
	(in thousands)	
Laboratory equipment	$ 19,675	$ 19,384
Leasehold improvements	12,554	15,695
Furniture and office equipment	2,333	2,524
Other	502	230
Total property and equipment	35,064	37,833
Less: accumulated depreciation	(17,207)	(15,913)
Property and equipment, net	$ 17,857	$ 21,920

The Company recorded $6.2 million, $5.2 million, and $3.8 million in depreciation expense during the years ended December 31, 2022, 2021, and 2020, respectively.

6. Accrued expenses

Accrued expenses consist of the following:

	As of December 31,	
	2022	2021
	(in thousands)	
Employee compensation costs	$ 4,559	$ 5,022
Research and development costs	1,895	3,719
Accrued goods and services	636	1,482
Professional services	726	727
Total	$ 7,816	$ 10,950

7. Lease obligation

Operating Leases

As of December 31, 2022, the Company has a lease for office and laboratory 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 laboratory 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 laboratory space at 75 Sidney Street (the "75 Sidney Street Lease"), effective immediately. 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 $1.5 million payable to its landlords as security for the performance of its obligations under the leases. These amounts are recorded as restricted cash and are included in deposits and other non-current assets in the accompanying consolidated balance sheets.

Total lease cost for operating leases of approximately $4.6 million, $6.8 million, and $6.2 million was incurred during the years ended December 31, 2022, 2021 and 2020, respectively. As of December 31, 2022, the weighted average remaining lease term was 6 years and the weighted average incremental borrowing rate used to determine the operating lease liabilities was 7.4%.

The following table summarizes the operating sublease income generated under the Sublease Agreement which was recorded within operating expenses for the years ended December 31, 2022 and 2021.

	Years ended December 31,	
	2022	2021
	(in thousands)	
Operating sublease income	$ 1,380	$ 838

8. Other liabilities

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

	As of December 31,	
	2022	2021
	(in thousands)	
Other current liabilities		
Lease liabilities	2,832	5,571
Total other current liabilities	$ 2,832	$ 5,571
Other non-current liabilities		
Lease liabilities	$ 20,294	$ 38,608
Other	1,001	1,001
Total other non-current liabilities	$ 21,295	$ 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. These costs are reported within our research and development expenses and general and administrative expenses. Substantially all costs have been paid as of December 31, 2022.

9. Commitments and contingencies

Significant Agreements

2019 Neurocrine Collaboration Agreement

Summary of Agreement

Effective March 2019, the Company entered into a collaboration agreement with Neurocrine (the "2019 Neurocrine Collaboration Agreement") for the research, development and commercialization of certain of its AAV gene therapy products. Under the 2019 Neurocrine Collaboration Agreement, the Company agreed to collaborate on the conduct of four collaboration programs (the "2019 Neurocrine Programs") which include: (a) VY-AADC (NBIb-1817) for Parkinson's disease (the "VY-AADC Program"), (b) VY-FXN01 for Friedreich's ataxia (the "FA Program") (collectively, with the VY-AADC Program, the "Legacy Programs"), and (c) two programs to be determined by the Company and Neurocrine at a later date (the "2019 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 2019 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 2019 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 2019 Neurocrine Collaboration Agreement.

In February 2021, Neurocrine notified the Company that it had elected to terminate the 2019 Neurocrine Collaboration Agreement solely with regards to the VY-AADC Program, effective August 2, 2021 (the "Neurocrine VY-AADC Program Termination Effective Date"). The 2019 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 2019 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 " 2019 Collaboration Products") under (a) the VY-AADC Program on a worldwide basis; (b) the FA Program in the United States and, all countries in the world in which the 2019 Neurocrine Collaboration Agreement remains in effect with respect to the FA Program; and (c) each 2019 Discovery Program on a worldwide basis. As a result of the termination of the 2019 Neurocrine Collaboration Agreement with regards to the VY-AADC Program, in accordance with the terms of the 2019 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 2019 Neurocrine Program prior to the occurrence of a specified event for such 2019 Neurocrine Program (a "2019 Transition Event"), as described below, and is required to use commercially reasonable efforts to develop the corresponding 2019 Collaboration Products. Neurocrine has agreed to be responsible for all costs incurred by the Company in conducting these activities for each 2019 Neurocrine Program, in accordance with an agreed budget for each 2019 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 2019 Neurocrine Program.

Upon the occurrence of a 2019 Transition Event for each 2019 Neurocrine Program, Neurocrine has agreed to assume responsibility for development, manufacturing and commercialization activities for such 2019 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 2019 Neurocrine Collaboration Agreement with respect to the VY-AADC Program, the 2019 Transition Event with respect to the VY-AADC Program is no longer applicable. The 2019 Transition Events for the remaining programs are (a) 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 (b) with respect to each 2019 Discovery Program, the preparation by the Company and the approval by Neurocrine of an IND application to be filed with the U.S. Food and Drug Administration (the "FDA") by Neurocrine for the first development candidate in such 2019 Discovery Program. For the FA Program, the Company was granted the option (the "2019 FA Co-Co Option") to co-develop and co-commercialize the FA Program upon the occurrence of a specified event (a "2019 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 "2019 FA Co-Co Agreement"), and (a) jointly develop and commercialize the 2019 Collaboration Products for the FA Program ("FA Collaboration Products"), (b) share in its costs, profits and losses, and (c) forfeit certain milestones and royalties on net sales in the United States during the effective period of the 2019 FA Co-Co Agreement. The 2019 FA Co-Co Trigger Event is the receipt of topline data for the initial Phase 1 clinical trial for a FA Program product candidate.

Under the 2019 Neurocrine Collaboration Agreement, subject to exceptions specified therein, the Company and Neurocrine agreed that profits and losses under the Company's 2019 FA Co-Co Option would be allocated 60% to Neurocrine and 40% to the Company for any FA Collaboration Product. The parties agreed that 2019 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 2019 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 2019 Neurocrine Collaboration Agreement.

Under the 2019 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 2019 Discovery

Programs. The Company and Neurocrine completed the nomination process, and the JSC has approved the two Targets for development under the 2019 Discovery Programs. The two Targets are currently under development.

The 2019 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 2019 Collaboration Products under (a) 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 2019 Neurocrine Collaboration Agreement; (b) the FA Program of up to $195.0 million, and (c) each of the two 2019 Discovery Programs of up to $130.0 million per 2019 Discovery Program. The Company may be entitled to receive aggregate commercial milestone payments for each 2019 Collaboration Product of up to $275.0 million, subject to an aggregate cap on commercial milestone payments across all 2019 Neurocrine Programs of $1.1 billion. Furthermore, in connection with the 2019 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 2019 Collaboration Products. Such royalty percentages, for net sales in and outside the United States, as applicable, range (a) for the VY-AADC Program, from the mid-teens to low thirties and the low-teens to low twenties, respectively, which the Company is no longer eligible to receive in light of the partial termination of the 2019 Neurocrine Collaboration Agreement; (b) for the FA Program, from the low-teens to high-teens and high-single digits to mid-teens, respectively; and (c) for each 2019 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 2019 Collaboration Product and terminate on the later of (a) the expiration of the last patent covering the 2019 Collaboration Product or its method of use in such country, (b) ten years from the first commercial sale of the 2019 Collaboration Product in such country and (c) the expiration of regulatory exclusivity in such country (the "2019 Royalty Term"). Royalty payments may be reduced by up to 50% in specified circumstances, including expiration of patents rights related to a 2019 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 2019 Collaboration Product. As a result of Neurocrine's termination of the 2019 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 2019 Royalty Term applicable to such 2019 Collaboration Product in such country.

Under the terms of the 2019 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 2019 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 2019 Collaboration Product is directed, subject to specified exceptions, including the parties' conduct of basic research activities.

Unless earlier terminated, the 2019 Neurocrine Collaboration Agreement expires on the later of (a) the expiration of the last to expire 2019 Royalty Term with respect to a 2019 Collaboration Product in all countries in the relevant territory or (b) the expiration or termination of any 2019 FA Co-Co Agreement. Neurocrine may terminate the 2019 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 2019 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 2019 Collaboration Product to which the termination applies. The Company may terminate the 2019 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 2019 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 2019 Neurocrine Program, if such termination were to occur after a 2019 Transition Event, then (a) with respect to the FA Program, if a 2019 FA Co-Co Agreement is in effect, Neurocrine can terminate the 2019 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 (b) subject to any license agreements, Neurocrine would no longer have any obligations with respect to any 2019 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 2019 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, and the provision of other information requested by the FDA for the RESTORE-1 Phase 2 clinical trial.

Accounting Analysis

At inception, the Company determined the 2019 Neurocrine Collaboration Agreement was a contract with a customer under ASC 606, and included the following performance obligations: (a) research and development services for each Legacy Program combined with a development and commercialization license for each such program and (b) research and development services for each 2019 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 2019 Transition Events associated with each 2019 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 revised the estimate of the expected reimbursement to approximately $80.0 million based on expectations as a result from decisions made at the JSC meeting held in the fourth quarter of 2021, which resulted in significantly less research and development services to be provided by the Company under the 2019 Neurocrine Collaboration Agreement. During the fourth quarter of 2022, the Company further revised the estimate of the expected reimbursement to approximately $81.7 million, based on expectations resulting from decisions made at the JSC meeting held in the fourth quarter of 2022. 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 total variable consideration allocated to each program related to the expected cost reimbursement was as follows as of December 31, 2022:

Performance Obligation	Amount
	(in thousands)
Variable Consideration	
VY-AADC Program	$ 53,863
FA Program	18,868
2019 Discovery Program 1	5,336
2019 Discovery Program 2	3,605
Total	$ 81,671

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

Performance Obligation	Amount
	(in thousands)
Fixed Consideration	
VY-AADC Program	$ 49,045
FA Program	20,647
2019 Discovery Program 1	14,443
2019 Discovery Program 2	8,247
Total	$ 92,382

The Company recognizes the transaction price associated with each performance obligation on a proportional performance basis over the period of service using input-based measurements such as costs incurred to date, to estimate proportion performed, and remeasures its progress towards completion at the end of each reporting period.

The Company determined the partial termination of the 2019 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 2019 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, 2019 Discovery Program 1 and 2019 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 years ended December 31, 2022 and 2021, the Company recognized $0.9 million and $37.4 million of revenue, respectively, associated with its collaboration with Neurocrine related to research and development services performed during the period and the corresponding cost reimbursement receivable. As of December 31, 2022, there was $11.8 million of deferred revenue related to the 2019 Neurocrine Collaboration Agreement, which is classified as either current or non-current in the accompanying consolidated balance sheet based on the period the services are expected to be delivered. Additionally, as of December 31, 2022, there was $0.3 million of collaboration receivables related to reimbursable costs expected to be received from Neurocrine for research and development services performed.

The following table presents changes in the balances of the Company's related party collaboration receivables and contract liabilities during the year ended December 31, 2022:

	Balance at December 31, 2021	Additions	Deductions	Balance at December 31, 2022
		(*in thousands*)		
Related party collaboration receivable	$ 732	$ 907	$ (1,382)	$ 257
Contract liabilities:				
Deferred revenue	$ 12,096	$ —	$ (269)	$ 11,827

The change in the receivables balance for the year ended December 31, 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 2019 Neurocrine Collaboration Agreement consist of internal and external research and development costs, which primarily include: salaries and benefits, laboratory supplies, preclinical research studies, clinical studies, consulting services, and commercial development. These costs are included in research and development expenses in the Company's consolidated statements of operations.

The Company incurred approximately $0.8 million of costs to obtain the 2019 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 Agreement"), pursuant to which the Company 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 Agreement, during an initial research term that ended as of October 1, 2022 (the "Pfizer Research Term"), Pfizer had the right to evaluate the potential use of the capsids in combination with up to two Pfizer Transgenes to help treat respective central nervous system ("CNS") and cardiovascular diseases.

During the Pfizer Research Term, the Company agreed to provide Pfizer with certain quantities of materials encoding specified existing capsids for Pfizer's evaluation. Further, during the Pfizer Research Term, the Company agreed to disclose to Pfizer, on a rolling basis, the performance characteristics identified during the Pfizer Research Term for all such capsid candidates. Pfizer had 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 had the right to exercise up to two Pfizer License Options, provided that it could exercise only one Pfizer License Option for each Pfizer Transgene.

Effective as of September 30, 2022, Pfizer exercised its Pfizer License Option with respect to a capsid for the specified Pfizer Transgene for potential treatment of a rare neurological disease. Pfizer did not exercise its option to license a capsid for the potential treatment of a cardiovascular disease. As result, Pfizer's right to exercise a Pfizer License Option for a cardiovascular disease has terminated in accordance with the terms of the Pfizer Agreement and all rights to capsids for that cardiovascular disease have reverted to the Company. Pfizer's exercise of a Pfizer License Option extends the Pfizer Research Term to October 1, 2024, during which period 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 the rare neurological disease associated with the exercise of the applicable Pfizer License Option.

Pursuant to the exercise of the Pfizer License Option, the Company granted Pfizer an exclusive, worldwide license, with the right to sublicense, under certain of the Company's intellectual property, the rights to develop and commercialize rare neurological disease products utilizing the capsid candidate and incorporating the corresponding Pfizer Transgene (the "Pfizer Licensed CNS Products"). Until October 1, 2024, while the Company is not obligated to conduct additional research activities to identify additional proprietary capsids that may be useful for AAV gene therapies for the treatment of rare neurological 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 Pfizer Research Term, conduct additional evaluations 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 Agreement, Pfizer is solely responsible for, and has sole decision-making authority with respect to, development and commercialization of the Pfizer Licensed CNS Products. Pfizer is required to use commercially reasonable efforts to develop and obtain regulatory approval for at least one Pfizer Licensed CNS Product for which Pfizer has exercised its Pfizer License Option in (a) the United States and (b) at least one of the following countries: the United Kingdom, France, Germany, Italy, Spain and Japan (each of which is referred to as a "Pfizer Major Market Country"), subject to certain limitations. Pfizer is also required to use commercially reasonable efforts to commercialize each Pfizer Licensed CNS 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 CNS Product, subject to certain limitations.

Under the terms of the Pfizer Agreement, Pfizer paid the Company an upfront payment of $30.0 million in October 2021. Following the exercise of the Pfizer License Option, Pfizer paid the Company a fee of $10.0 million and 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 CNS Product to achieve the corresponding milestone. On a Pfizer Licensed CNS Product-by-Pfizer Licensed CNS 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 CNS Product and (b) tiered, escalating royalties in the mid- to high-single-digit percentages of annual net sales of each Pfizer Licensed CNS 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 Agreement, each of 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 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 Agreement and in the course of the Company's and Pfizer's activities under the Pfizer Agreement will follow inventorship under U.S. patent law. Subject to certain limitations and exceptions, the Company agreed (a) during the Pfizer 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 (b) 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 Agreement expires on the expiration of the last-to-expire royalty term with respect to all Pfizer Licensed CNS Products in all countries. Subject to a cure period, either party may terminate the Pfizer 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 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 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 license that the Company has granted to Pfizer under the Pfizer Agreement shall become irrevocable and perpetual, and all milestone payments and royalties that would have otherwise been payable by Pfizer under such license had the Pfizer Agreement remained in effect would be substantially reduced.

Accounting Analysis

At inception, the Company determined the Pfizer Agreement was a contract with a customer under ASC 606. The Company assessed the promised goods and services under the Pfizer Agreement, in accordance with ASC 606, and determined that the Pfizer 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 evaluations 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 Agreement, which represents the transaction price at inception. Additional consideration to be paid to the Company upon exercise of the Pfizer License Option 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 Pfizer License Options 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 (a) the downstream economics including option fees, milestones and royalties related to each Pfizer License Option being identical and (b) 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 was $15.0 million for each material right. The amount allocated to each material right was initially recorded as deferred revenue.

During the year ended December 31, 2022, the Company recognized $40.0 million in collaboration revenue related to the Pfizer Agreement. Of this $40.0 million, $25.0 million is attributable to the exercise of the first material right for the Pfizer License Option for a rare neurological disease and includes the option exercise fee of $10.0 million. The remaining $15.0 million is attributable to the expiration of the second material right associated with the Pfizer License Option for a cardiovascular disease.

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 Agreement"). Pursuant to the Novartis 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, on a target-by-target basis (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 up to 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, as applicable, 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 applicable 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 applicable 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.

Effective as of March 1, 2023, Novartis exercised its Novartis License Options to license novel capsids generated from the Company's TRACER capsid discovery platform for use in gene therapy programs against two undisclosed Initial Novartis Targets. For more information, refer to Note 15 to the Company's consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

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 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 (a) the United States and (b) 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 Agreement, Novartis paid the Company an upfront payment of $54.0 million. Effective as of March 1, 2023, Novartis exercised its Novartis License Options to license novel capsids generated from the Company's TRACER capsid discovery platform for use in gene therapy programs against two undisclosed Initial Novartis Targets. For more information, refer to Note 15 to the Company's consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Under the terms of the Novartis 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 Agreement and in the course of the parties' activities under the Novartis Agreement will follow inventorship under U.S. patent law.

Subject to certain limitations and exceptions, the Company has agreed (a) 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 (b) 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 Agreement expires on the expiration of the last-to-expire royalty term with respect to all Novartis Licensed Products in all countries. Subject to a cure period, either party may terminate the Novartis 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 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 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 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 Agreement remained in effect would be substantially reduced.

Accounting Analysis

At inception, the Company determined the Novartis Agreement was a contract with a customer under ASC 606. The Company assessed the promised goods and services and determined that the Novartis 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 and when exercised.

The Company received a nonrefundable, upfront payment of $54.0 million as consideration under the Novartis 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 was recognized upon the exercise of two Novartis License Options in 2023 and upon the expiration of the remaining Novartis License Option in 2023.

During the year ended December 31, 2022, the Company did not recognize any revenue related to the Novartis Agreement. As of December 31, 2022, the entire transaction price of $54.0 million is recorded as deferred revenue, current in the accompanying consolidated balance sheet.

License Agreement with Touchlight IP Limited

On November 3, 2022, the Company and Touchlight IP Limited ("Touchlight") entered into a license agreement (the "Touchlight License Agreement") to authorize historical use by the Company of a certain DNA preparation process ("Subject DNA Preparation Process"), and to authorize the prospective exploitation of TRACER Capsids created with the use of the Subject DNA Preparation Process.

The terms of the Touchlight License Agreement include a one-time, non-refundable technology access fee of $5.0 million, which was paid during the fourth quarter of 2022. The Company recorded the $5.0 million to research and development expense in the year ended December 31, 2022, accordingly.

The terms of the Touchlight License Agreement also include future milestone payments and low single-digit royalties payable to Touchlight if the Company or its program collaborators or licensees choose to utilize in a therapeutic product TRACER Capsids that were created with the historical use of the Subject DNA Preparation Process. Additionally, the Company is obligated to pay low single-digit royalties to Touchlight on future payments the Company receives in connection with licensing of TRACER capsids that were created with the historical use of the Subject DNA Preparation Process, excluding the licensing of or collaboration on any Company therapeutic programs. No milestone or royalty payments were due and payable as of December 31, 2022.

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 evaluated the arrangement and 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 for the year ended December 31, 2017 is recorded as a non-current liability in the consolidated balance sheet.

Litigation

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

10. Common stock

As of December 31, 2022 and 2021, the Company had authorized 120,000,000 shares of common stock, at $0.001 par value per share.

General

The voting, dividend and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers and preferences of the holders of preferred stock. The common stock has the following characteristics:

Liquidation

The holders of shares of common stock are entitled to share ratably in the Company's remaining assets available for distribution to its stockholders in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon occurrence of a deemed liquidation event.

Shares Reserved For Future Issuance

	As of December 31,	
	2022	2021
Shares reserved for vesting of restricted stock awards under the Founder Agreements	45,000	137,255
Shares reserved for exercise of outstanding stock options	6,199,571	5,013,193
Shares reserved for vesting of outstanding restricted stock units	1,112,563	806,379
Shares reserved for issuances under the 2015 Stock Option Plan	3,536,932	4,374,539
Shares reserved for issuances under the 2015 Employee Stock Purchase Plan	1,884,309	1,659,574
	12,778,375	11,990,940

11. Stock-based compensation

2014 Stock Option and Grant Plan

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

The terms of stock option agreements, including vesting requirements, were determined by the Board of Directors and were subject to the provisions of the 2014 Plan. Restricted stock awards granted by the Company generally vest based on each grantee's continued service with the Company during a specified period following grant. Stock options granted to employees generally vest over four years, with 25% vesting on the one year anniversary and 75% vesting ratably, on a monthly basis, over the remaining three years. Stock options granted to non-employee consultants generally vest monthly over a period of one to four years.

Founder Awards

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

The remainder of the restricted stock awards were slated to vest upon the achievement of certain performance objectives as well as continued service to the Company, as set forth in the agreements. Stock-based compensation expense associated with these performance-based awards is recognized when the achievement of the performance condition is considered probable, using management's best estimates. The Company has modified certain of the awards, including repurchasing a total of 131,470 shares underlying the awards through December 31, 2022, and modifying the vesting provisions such that the modified awards vest over time rather than based on performance. The stock-based compensation expense recorded related to these awards during the years ended December 31, 2022, 2021, and 2020 were immaterial to the Company's consolidated financial statements.

2015 Stock Option Plan

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

Effective January 1, 2016 and every anniversary thereafter an additional 4% of outstanding common stock was added to the Company's 2015 Stock Option Plan pursuant to its "evergreen" provision, for future issuance. This has accumulated to a total of 10,771,368 shares through January 1, 2023. During the year ended December 31, 2022, the Company granted options to purchase 3,291,075 shares of common stock to employees and directors under the 2015 Stock Option Plan. As of December 31, 2022, there were 3,536,932 shares available for future issuance under the 2015 Stock Option Plan.

2015 Employee Stock Purchase Plan

In October 2015, the Company's board of directors and stockholders approved the 2015 Employee Stock Purchase Plan (the "2015 ESPP"). Under the 2015 ESPP, all full-time employees of the Company are eligible to purchase common stock of the Company twice per year, at the end of each six-month payment period. During each payment period, eligible employees who so elect, may authorize payroll deductions in an amount of 1% to 10% (whole percentages only) of the employee's base pay for each payroll period. At the end of each payment period, the

accumulated deductions are used to purchase shares of common stock from the Company at a discount. A total of 262,362 shares of common stock were initially authorized for issuance under this plan.

The 2015 ESPP became effective upon the completion of the IPO. Effective January 1, 2016 and every anniversary thereafter an additional 1% of outstanding common stock was added to the 2015 ESPP, pursuant to its evergreen provision, for future issuance. This has accumulated to a total of 2,692,838 shares through January 1, 2023. The Company issued 150,265 and 200,006 shares of common stock under the 2015 ESPP in the years ended December 31, 2022 and 2021. As of December 31, 2022, there were 1,884,309 shares available for future purchase under the 2015 ESPP.

Inducement Awards

In the years ended December 31, 2022, 2021, and 2020, the Company issued non-statutory stock options to purchase an aggregate of 390,000, 76,500 and 172,500 shares of the Company's common stock and restricted stock unit awards for an aggregate of 163,000, 13,000 and 29,000 shares of the Company's common stock, respectively, in each case outside of the Company's 2015 Stock Option Plan as an inducement material to certain individuals' acceptance of an offer of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

The stock options will vest over a four-year period, with 25% of the shares underlying the option award vesting on the first anniversary of the award and the remaining 75% of the shares underlying the award vesting monthly thereafter over the subsequent 36-month period. The restricted stock units vest over a three-year period, with 33% of the restricted stock units vesting on the first anniversary of the award, 33% of the restricted stock units vesting on the second anniversary, and the remaining restricted stock units vesting on the third anniversary.

Stock-based Compensation Expense

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

	Year ended December 31,		
	2022	2021	2020
	(in thousands)		
General and administrative	$ 6,398	$ 7,191	$ 8,577
Research and development	2,946	4,133	6,357
Total stock-based compensation expense	$ 9,344	$ 11,324	$ 14,934

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

	Year ended December 31,		
	2022	2021	2020
	(in thousands)		
Stock options	$ 5,938	$ 7,438	$ 11,387
Restricted stock awards and units	3,215	3,551	3,110
Employee stock purchase plan awards	191	335	437
Total stock-based compensation expense	$ 9,344	$ 11,324	$ 14,934

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 year ended December 31, 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
Awarded	964,480	$ 4.29
Vested	(436,611)	$ 6.92
Forfeited	(221,685)	$ 5.05
Unvested restricted stock units as of December 31, 2022	1,112,563	$ 5.27

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 recognized over the vesting period. In the year ended December 31, 2022, the Company granted 864,480 restricted stock units vesting in equal amounts, annually over three years, and 100,000 restricted stock units vesting in equal amounts, annually over four years. The stock-based compensation expense was $2.9 million, $3.3 million, and $2.8 million for the years ended December 31, 2022, 2021, and 2020, respectively.

As of December 31, 2022, the Company had unrecognized stock-based compensation expense related to its unvested restricted stock units of $3.7 million which is expected to be recognized over the remaining weighted average vesting period of 1.9 years.

Stock Options

A summary of the status of, and changes in, stock options was as follows:

	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		
Granted	3,681,075	$ 5.17		
Exercised	(89,012)	$ 7.07		
Cancelled or forfeited	(2,405,685)	$ 13.15		
Outstanding at December 31, 2022	6,199,571	$ 8.12	7.9	$ 6,095
Exercisable at December 31, 2022	2,744,489	$ 10.56	6.5	$ 2,287

Using the Black-Scholes option pricing model, the weighted average fair value of options granted during the year ended December 31, 2022 was $3.60. The stock-based compensation expense related to stock option awards granted was $5.8 million, $7.3 million, and $11.2 million for the years ended December 31, 2022, 2021, and 2020, respectively.

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

	Year ended December 31,		
	2022	2021	2020
Risk-free interest rate	2.2 %	0.9 %	1.0 %
Expected dividend yield	— %	— %	— %
Expected term (in years)	6.0	6.0	6.0
Expected volatility	79.4 %	75.0 %	73.7 %

As of December 31, 2022, the Company had unrecognized stock-based compensation expense related to its unvested stock options of $12.8 million which is expected to be recognized over the remaining weighted average vesting period of 2.9 years.

12. 401(k) Savings plan

The Company has a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pretax basis. The Company expensed approximately $0.9 million, $1.1 million, and $1.1 million related to employer contributions made during the years ended December 31, 2022, 2021, and 2020, respectively.

13. Income taxes

The Company recognized deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the Company's financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all the deferred tax assets will not be realized. The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position. The Company evaluates its tax positions on an annual basis. The provision for incomes taxes is as follows:

	Year ended December 31,		
	2022	2021	2020
	(in thousands)		
Current			
Federal	$ —	$ —	$ —
State	16	—	—
Total current	16	—	—
Deferred			
Federal	—	—	—
State	—	—	—
Total deferred	—	—	—
Total tax provision	$ 16	$ —	$ —

A reconciliation of the expected income tax provision computed using the federal statutory income tax rate at the Company's effective tax rate for the years ended December 31, 2022, 2021, and 2020 is as follows:

	Year ended December 31,		
	2022	2021	2020
Income tax computed at federal statutory tax rate	21.0 %	21.0 %	21.0 %
State taxes, net of federal benefit	5.2 %	6.6 %	(2.3)%
Provision to return	3.2 %	4.9 %	— %
General business credit carryovers	(3.5)%	3.2 %	(20.6)%
Non-deductible expenses	(4.6)%	(3.8)%	5.0 %
Other	— %	— %	1.9 %
Change in valuation allowance	(21.3)%	(31.9)%	(5.0)%
Total	— %	— %	— %

The Company has historically incurred net operating losses ("NOLs"). As of December 31, 2022, the Company had federal and state net operating loss carryforwards of $175.1 million and $166.5 million, respectively. As of December 31, 2022, the Company had federal and state research and development tax credit carryforwards of $24.0 million and $9.6 million, respectively, which expire beginning in 2033. As of December 31, 2021, the Company had state investment credits of $0.5 million, which expire beginning in 2023.

The significant components of the Company's deferred tax assets and (liabilities) as of December 31, 2022 and 2021 are as follows:

	As of December 31,	
	2022	2021
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforward	$ 47,282	$ 56,756
Tax credit carryforward	32,060	30,122
Lease liability	6,318	12,012
Deferred revenue	17,984	11,485
Stock compensation	4,630	7,784
Non-deductible accruals and reserves	1,603	1,507
Capitalized research expenses	14,351	—
Intangibles	610	664
Other temporary differences	(1)	—
Total deferred tax assets	124,837	120,330
Less valuation allowance	(117,416)	(107,563)
Net deferred tax assets	7,421	12,767
Deferred tax liabilities		
Right of use assets	(4,231)	(9,128)
Depreciation and amortization	(3,190)	(3,632)
Other temporary differences	—	(7)
Net deferred taxes	$ —	$ —

As required by ASC 740, management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which principally comprise NOL carryforwards, research and development credit carryforwards, and lease liability. Management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets, and as a result, a valuation allowance of $117.4 million and $107.6 million has been established at December 31, 2022 and 2021, respectively. The change in valuation allowance was $9.8 million for the year ended December 31, 2022. The primary reason for the difference between the income tax provision recorded by the Company and the amount of income tax provision at statutory income tax rates was the change in the valuation allowance.

At December 31, 2022 and 2021, the Company had no unrecognized tax benefits. The Company has not as yet conducted a study of its research and development credit carryforwards. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheets or statements of operations if an adjustment were required.

Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the accompanying statements of operations. As of December 31, 2022 and 2021, the Company has no accrued interest related to uncertain tax positions. Since the Company is in a loss carryforward position, it is generally subject to examination by the U.S. federal, state, and local income tax authorities for all tax years in which a loss carryforward is available.

14. Related-party transactions

During the years ended December 31, 2022, 2021, and 2020, the Company received board and scientific advisory services from two of its prior executives, Steven M. Paul, M.D., the Company's former President and Chief Executive Officer, and Dinah Sah, Ph.D., the Company's former Chief Scientific Officer. As of December 31, 2020, Dr. Paul's consulting agreement was complete. The total amount of fees paid to Dr. Paul for services provided during the year ended December 31, 2020 was $0.2 million. The total amount of fees paid to Dr. Sah for services provided during the years ended December 31, 2022, 2021 and 2020 was $0.5 million, $0.2 million, and $0.4 million, respectively.

During the year ended December 31, 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 year ended December 31, 2022.

Under the 2019 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 9). Amounts due from Neurocrine are reflected as related party collaboration receivables. As of December 31, 2022, the Company recorded approximately $0.3 million in related party collaboration receivables.

15. Subsequent events

2023 Neurocrine Collaboration

On January 8, 2023, the Company entered into the 2023 Neurocrine Collaboration Agreement, with Neurocrine for the research, development, manufacture and commercialization of gene therapy products directed to the gene that encodes glucosylceramidase beta 1 ("GBA1") for the treatment of Parkinson's disease and other diseases associated with GBA1 (the "GBA1 Program") and three new programs focused on the research, development, manufacture and commercialization of gene therapies designed to address central nervous system diseases or conditions associated with rare genetic targets (the "2023 Discovery Programs" and, collectively with the GBA1 Program, the "2023 Neurocrine Programs").

Under the terms of the 2023 Neurocrine Collaboration Agreement, Neurocrine paid to the Company an upfront payment of approximately $136.0 million (the "Upfront Collaboration Payment") and approximately $39.0 million as consideration (the "Share Consideration") for an equity purchase of 4,395,588 shares of the Company's common stock (the "Shares") in February 2023. The 2023 Collaboration Agreement also provides for aggregate development milestone payments from Neurocrine for gene therapy products arising under the 2023 Neurocrine Programs (the "2023 Collaboration Products") under (a) the GBA1 Program of up to $985.0 million; and (b) each of the three 2023 Discovery Programs of up to $175.0 million for each 2023 Discovery Program. The Company may be entitled to receive aggregate commercial milestone payments for up to two 2023 Collaboration Products under the GBA1 Program of up to $950.0 million per 2023 Collaboration Product and for one 2023 Collaboration Product under each 2023 Discovery Program of up to $275.0 million per 2023 Discovery Program.

The 2023 Neurocrine Collaboration Agreement became effective on February 21, 2023, upon expiration of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended. On February 23, 2023, the Company received the Upfront Collaboration Agreement and the Share Consideration and issued and sold to Neurocrine the Shares pursuant to the applicable stock purchase agreement.

In connection with the execution of the 2023 Neurocrine Collaboration Agreement, the Company amended and restated their existing investor agreement on January 8, 2023 (the "2023 Neurocrine Amended and Restated Investor Agreement"), providing for standstill and lock-up restrictions and a voting agreement with respect to shares of the Company owned by Neurocrine.

Novartis Option Exercises

Effective as of March 1, 2023, Novartis exercised its Novartis License Options to license novel capsids generated from the Company's TRACER capsid discovery platform for use in gene therapy programs against two undisclosed Initial Novartis Targets. With Novartis' option exercise on two Initial Novartis Targets, the Company will receive a $25.0 million option exercise payment during the first half of 2023, and is eligible to receive associated potential development, regulatory, and commercial milestone payments, as well as mid- to high-single-digit tiered royalties based on net sales of the Novartis Licensed Products incorporating the Novartis Licensed Capsids. The two Initial Novartis Targets licensed are distinct from targets in the Company's internal and partnered pipeline. In addition, over the next 18 months, Novartis retains the right to expand the agreement to include options to license capsids for up to two Additional Novartis Targets, subject to their availability, for a fee of $18.0 million per Additional Novartis Target. Under such an expansion, the Company would be eligible to receive a $12.5 million license option exercise fee for each Additional Novartis Target exercised, as well as future potential milestone payments per Additional Novartis Target and tiered mid- to high-single digit royalties on the Novartis Licensed Products incorporating the Novartis Licensed Capsids.

Novartis elected not to license a capsid for one Initial Novartis Target under the Novartis Agreement prior to the expiration of the applicable Novartis License Option. As a result, the non-exclusive research license that we granted to Novartis in connection with this Initial Novartis Target has terminated, the Novartis Research Term for this Initial Novartis Target has expired, and we are no longer eligible to receive development, regulatory, and commercial milestone payments or royalties in connection with this Initial Novartis Target. All capsid rights with respect to that Initial Novartis Target have returned to the Company.

EXHIBIT INDEX

Exhibit No.	Description	Incorporated by Reference to:				Filed Herewith
		Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number	
3.1	Amended and Restated Certificate of Incorporation of the Registrant	8-K	3.1	11/16/2015	001-37625	
3.2	Amended and Restated By-Laws of the Registrant	8-K	3.2	11/16/2015	001-37625	
4.1	Specimen Common Stock Certificate of the Registrant	10-K	4.1	03/14/2018	001-37625	
4.4	Description of Registrant's Securities	10-K	4.4	03/03/2020	001-37625	
10.1#	2014 Stock Option and Grant Plan and forms of award agreements thereunder	S-1/A	10.1	10/28/2015	333-207367	
10.2#	2015 Stock Option and Incentive Plan and forms of award agreements thereunder	S-1/A	10.2	10/28/2015	333-207367	
10.3†	Collaboration Agreement, by and between the Registrant and Sanofi Genzyme Corporation, dated February 11, 2015	S-1/A	10.3	11/06/2015	333-207367	
10.4*	Termination Agreement, by and between the Registrant and Genzyme Corporation, dated June 14, 2019	10-Q	10.3	08/09/2019	001-37625	
10.5*	Amended and Restated Option and License Agreement, by and between the Registrant and Genzyme Corporation, dated June 14, 2019	10-Q	10.4	08/09/2019	001-37625	
10.6*	First Amendment to Amended and Restated Option and License Agreement with Genzyme Corporation, dated September 20, 2020	10-Q	10.1	11/09/2020	001-37625	
10.7†	Collaboration and License Agreement, by and between the Registrant and Neurocrine Biosciences, Inc., dated January 28, 2019	10-K	10.28	02/26/2019	001-37625	
10.8	Amendment No. 1 to the Collaboration and License Agreement, by and between the Registrant and Neurocrine Biosciences, Inc., dated June 14, 2019	10-Q	10.5	08/09/2019	001-37625	
10.09*	Option and License Agreement, by and between the Registrant and Pfizer Inc., dated October 1, 2021	10-Q	10.2	11/02/21	001-37625	

10.10	Lease Agreement, by and between the Registrant and UP 45/75 Sidney Street, LLC, dated April 1, 2014	S-1/A	10.5	10/28/2015	333-207367
10.11	First Amendment to the Lease Agreement, by and between the Registrant and UP 45/75 Sidney Street, LLC, dated December 23, 2015	10-Q	10.5	05/12/2016	001-37625
10.12	Second Amendment to the Lease Agreement, by and between the Registrant and UP 45/75 Sidney Street, LLC, dated February 5, 2018	8-K	10.1	02/07/2018	001-37625
10.13	Third Amendment to the Lease Agreement, by and between the Registrant and UP 45/75 Sidney Street, LLC, dated June 1, 2018	8-K	10.1	06/05/2018	001-37625
10.14	Sublease Agreement, by and between Registrant and BioNTech US Inc., dated September 3, 2021	10-Q	10.1	11/02/2021	001-37625
10.15	Lease Agreement, by and between the Registrant and UP 64 Sidney Street, LLC, dated December 23, 2015	10-Q	10.6	05/12/2016	001-37625
10.16	First Amendment to the Lease Agreement, by and between the Registrant and UP 64 Sidney Street, LLC, dated June 1, 2018	8-K	10.2	06/05/2018	001-37625
10.17	Lease Agreement, by and between the Registrant and HCP/King 75 Hayden LLC, dated March 16, 2020	8-K	10.1	03/19/2020	001-37625
10.18	Form of Indemnification Agreement to be entered into between the Registrant and its directors	S-1/A	10.9	10/28/2015	333-207367
10.19	Form of Indemnification Agreement to be entered into between the Registrant and its executive officers	S-1/A	10.10	10/28/2015	333-207367
10.20#	2015 Employee Stock Purchase Plan	S-1/A	10.12	10/28/2015	333-207367
10.21#	Amendment No. 1 to the 2015 Employee Stock Purchase Plan	10-K	10.21	03/14/2018	001-37625
10.22#	Retirement Agreement, by and between the Registrant and Dinah Sah, Ph.D., dated May 20, 2019	8-K	10.1	05/21/2019	001-37625

10.23#	Employment Agreement, by and between the Registrant and Michael Higgins, dated May 19, 2021	8-K	10.2	05/19/2021	001-37625
10.24#	Employment Agreement, by and between the Registrant and Glenn Pierce, M.D., Ph.D., dated May 19, 2021	8-K	10.3	05/19/2021	001-37625
10.25#	Amendment No. 1 to Employment Agreement, by and between the Registrant and Glenn Pierce, dated June 7, 2021	8-K	10.1	06/08/2021	001-37625
10.26#	Employment Agreement, by and between the Registrant and Robert W. Hesslein, dated January 15, 2019	10-Q	10.5	05/07/2019	001-37625
10.27#	Amended and Restated Employment Agreement, by and between the Registrant and Robin Swartz, effective as of February 7, 2022	8-K	10.2	02/03/2022	001-37625
10.28#	Consulting Agreement, by and between the Registrant and Dinah Sah, Ph.D., dated June 28, 2019	10-Q	10.6	08/09/2019	001-37625
10.29#	Amendment No. 1 to the Consulting Agreement, by and between the Registrant and Dinah Sah, Ph.D., dated September 16, 2019	10-Q	10.2	11/06/2019	001-37625
10.30#	Consulting Agreement by and between the Registrant and Alfred Sandrock, effective as of February 7, 2022	8-K	10.1	02/03/2022	001-37625
10.31#	Form of Non-Qualified Stock Option Agreement for Inducement	10-K	10.27	02/26/2019	001-37625
10.32#	Form of Restricted Stock Unit Agreement for Inducement	10-K	10.33	02/26/2019	001-37625
10.33	Sales Agreement, by and between the Registrant and Cowen and Company, LLC, dated November 8, 2022	S-3	1.2	11/08/2022	333-268240
10.34#	Consulting Agreement by and between the Registrant and Allison Dorval, dated as of November 26, 2021	10-K	10.38	03/08/2022	001-37625
10.35*	Consulting Agreement by and between the Registrant and Alfred Sandrock, effective as of February 7, 2022	8-K	10.1	02/03/2022	001-37625

10.36	Option and License Agreement by and between the Registrant and Novartis Pharma AG, dated March 4, 2022					X
10.37#	Employment Agreement, by and between the Registrant and Alfred Sandrock, M.D., Ph.D., effective as of March 22, 2022.	8-K	10.1	03/22/2022	001-37625	
10.38#	Consulting Agreement by and between the Registrant and Glenn Pierce, M.D., Ph.D., effective as of June 6, 2022	8-K	10.1	06/07/2022	001-37625	
10.39	Lease Termination Agreement by and between the Registrant and BRE-BMR Pilgrim & Sidney LLC, dated as of June 22, 2022	8-K	10.1	06/23/2022	001-37625	
10.40	Sublease Termination Agreement by and between the Registrant and BioNTech US, Inc., dated as of June 22, 2022	8-K	10.2	06/23/2022	001-37625	
10.41	Employment Agreement by and between the Registrant and Peter Pfreundschuh, effective as of September 7, 2022	8-K	10.1	09/07/2022	001-37625	
10.42	Second Amended and Restated Employment Agreement by and between the Registrant and Todd Carter, Ph.D., effective as of September 7, 2022	8-K	10.2	09/07/2022	001-37625	
10.43	Patent and Know-How Licence between the Registrant and Touchlight IP Limited, dated as of November 3, 2022					X
10.44	Stock Purchase Agreement by and between the Registrant and Neurocrine Biosciences, Inc., dated as of January 8, 2023					X
10.45	Collaboration and License Agreement by and between the Registrant and Neurocrine Biosciences, Inc., dated as of January 8, 2023					X
10.46	Amended and Restated Investor Agreement by and between the Registrant and Neurocrine Biosciences, Inc., dated as of January 8, 2023					X
10.47#	Transition, Separation and Release of Claims Agreement, by and between the Company and Robert W. Hesslein, dated February 22, 2023.	8-K	10.1	02/23/2023	001-37625	
21.1	Subsidiaries of the Registrant.					X

23.1	Consent of Ernst & Young, Independent Registered Public Accounting Firm.	X
24.1	Power of Attorney (see signature page of this Annual Report on Form 10-K).	X
31.1	Certification of Principal Executive Officer pursuant to Exchange Act Rules 13a-14 or 15d-14.	X
31.2	Certification of Principal Financial Officer pursuant to Exchange Act Rules 13a-14 or 15d-14.	X
32.1+	Certifications of Principal Executive Officer and Principal Financial Officer pursuant to Exchange Act Rules 13a-14(b) or 15d-14(b) and 18 U.S.C. Section 1350.	X
101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document.	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Document.	X
101.LAB	Inline XBRL Taxonomy Extension Definition Linkbase Document.	X
101.PRE	Inline XBRL Taxonomy Extension Labels Linkbase Document.	X
101.DEF	Inline XBRL Taxonomy Extension Presentation Link 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	

Management contract or compensatory plan or arrangement filed in response to Item 15(a)(3) of the Instructions to the Annual Report on Form 10-K.

† Confidential treatment has been granted as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.

* Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K

+ The certification furnished in Exhibit 32.1 hereto is deemed to be furnished with this Annual Report on Form 10-K 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 Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

March 7, 2023

VOYAGER THERAPEUTICS, INC.

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

Alfred Sandrock, M.D., Ph.D.

Chief Executive Officer, President, and Director

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned directors and officers of Voyager Therapeutics, Inc. (the "Company"), hereby severally constitute and appoint Alfred Sandrock and Peter Pfreundschuh, and each of them singly, our true and lawful attorneys, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed by the following persons in the capacities and on the dates indicated.

Name	Title	Date
/s/Alfred Sandrock, M.D., Ph.D. Alfred Sandrock, M.D., Ph.D.	Chief Executive Officer, President, and Director *(Principal Executive Officer)*	March 7, 2023
/s/Peter P. Pfreundschuh Peter P. Pfreundschuh	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 7, 2023
/s/Michael Higgins Michael Higgins	Director (Chairman of the Board)	March 7, 2023
/s/Grace E. Colón, Ph.D. Grace E. Colón, Ph.D.	Director	March 7, 2023
/s/Jim Geraghty Jim Geraghty	Director	March 7, 2023
/s/Steven Hyman, M.D. Steven Hyman, M.D.	Director	March 7, 2023
/s/Catherine J. Mackey, Ph.D. Catherine J. Mackey, Ph.D.	Director	March 7, 2023
/s/Jude Onyia, Ph.D. Jude Onyia, Ph.D.	*Director*	March 7, 2023
/s/Glenn Pierce, M.D., Ph.D. Glenn Pierce, M.D., Ph.D.	Director	March 7, 2023
/s/Nancy Vitale Nancy Vitale	Director	March 7, 2023

XBRL-Only Content Section

Element	Value	
dei:EntityCentralIndexKey#	0001640266	
deiDocumentFiscalPeriodFocus	FY	
dei:AmendmentFlag	False	

LEADERSHIP TEAM

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

Todd Carter
Chief Scientific Officer

Robert W. Hesslein*
General Counsel

Trista Morrison
Chief of Staff, SVP Corporate Affairs

Allen Nunnally*
Chief Business Officer

Peter P. Pfreundschuh
Chief Financial Officer

Michelle Quinn Smith
Chief Human Resources Officer

Robin Swartz
Chief Operating Officer

**Outgoing officer/leadership team member*

BOARD OF DIRECTORS

Michael Higgins *(Chair)*

Board Member: Pulmatrix, Inc. *(Chair)*; Nocion Therapeutics, Inc.; Camp4 Therapeutics Corporation; Sea Pharmaceuticals, LLC; KinDex Pharmaceuticals, Inc.

Grace E. Colón, Ph.D.

Board Member: CareDx, Inc.; ProterixBio, Inc. *(Executive Chair)*; Massachusetts Institute of Technology (MIT) Corp. *(term member)*; Biotechnology Innovation Organization

James A. Geraghty

Chairman of the Board of Directors: Orchard Therapeutics PLC; Pieris Pharmaceuticals, Inc.

Board Member: Fulcrum Therapeutics, Inc.

Steven Hyman, M.D.

Board Member: Cyclerion Therapeutics, Inc.; Stanley Center for Psychiatric Research at the Broad Institute of Harvard and MIT

Faculty Member, Broad Institute

Distinguished Service Professor of Stem Cell and Regenerative Biology, Harvard University

Catherine J. Mackey, Ph.D.

Board Member: Avid Bioservices, Inc.; IDEAYA Biosciences, Inc.; Rady Children's Hospital; Rady Children's Institute for Genomic Medicine

Jude Onyia, Ph.D.

Chief Scientific Officer, Neurocrine Biosciences, Inc.

Glenn Pierce, M.D., Ph.D.

Board Member: World Federation of Hemophilia

Entrepreneur-in-Residence, Third Rock Ventures

Consultant: Voyager Therapeutics, Inc.

Alfred Sandrock, M.D., Ph.D.

Director, President and Chief Executive Officer, Voyager Therapeutics, Inc.

Board Member: Verge Genomics, Inc.; Atalanta Therapeutics, Inc.; Transition Bio, Inc.; Neurimmune AG

Nancy Vitale

Chief People Officer, Omada Health, Inc.

Voyager Therapeutics, Inc.
64 Sidney Street
Cambridge, MA 02139

voyager THERAPEUTICS

Legal Counsel
Wilmer Cutler Pickering Hale and Dorr LLP; Boston, MA / New York, NY

Independent Auditors
Ernst & Young LLP; Boston, MA

Transfer Agent and Registrar
Computershare Trust Company, N.A.; Canton, MA

Annual Meeting
The Annual Meeting of Stockholders will be held June 6, 2023, 9:00 am ET