voyager
therapeutics

2024 ANNUAL REPORT

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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, 2024

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.)**
75 Hayden Avenue, Lexington, Massachusetts	**02421**
(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 28, 2024, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $407.6 million (based on the last reported sale price on the Nasdaq Global Select Market as of such date).

As of March 3, 2025, there were 55,206,885 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 2025 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 proprietary adeno-associated virus, or AAV, gene therapy, antibody, and non-viral therapeutic product candidates;
- our ability to continue to develop our proprietary gene therapy platform technologies, including our TRACER™ (Tropism Redirection of AAV by Cell-type-specific Expression of RNA) discovery platform, our vectorized antibody platform, our non-viral therapeutics platform, and our proprietary antibody, gene therapy, vectorized antibody, and non-viral therapeutic programs;
- our ability to identify and optimize product candidates, proprietary AAV capsids, and non-viral blood-brain-barrier shuttles;
- our strategic collaborations and licensing agreements with, and funding from, our collaboration partners Neurocrine Biosciences, Inc. and Novartis Pharma AG, or Novartis, and our licensee Alexion, AstraZeneca Rare Disease (successor-in-interest to former licensee Pfizer Inc.);
- our ongoing and planned clinical trials, 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 submit investigational new drug, or IND, applications for our programs;
- our estimates regarding future revenue, expenses, contingent liabilities, existing cash resources, capital requirements and cash runway;
- 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 might 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 and platform development objectives 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, licenses, joint ventures or investments we may make or enter into.

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.

We obtained the statistical and other industry and market data in this Annual Report on Form 10-K and the documents we have filed as exhibits to the Annual Report on Form 10-K from our own internal estimates and research, as well as from industry and general publications and research, surveys, studies and trials conducted by third parties. Some data is also based on our good faith estimates, which are derived from management's knowledge of the industry and independent sources. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, while we believe the market opportunity information included in this Annual Report on Form 10-K and the documents we have filed as exhibits to the Annual Report on Form 10-K is reliable and is based upon reasonable assumptions, such data involves risks and uncertainties and are subject to change based on various factors, including those discussed under "Risk Factors" and in the documents we have filed as exhibits to the Annual Report on Form 10-K. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely upon these statements.

We own various U.S. federal trademark registrations and applications and unregistered trademarks, including our corporate logo. This Annual Report on Form 10-K and the documents filed as exhibits to the Annual Report on Form 10-K contain references to trademarks, service marks and trade names referred to in this Annual Report on Form 10-K and the information incorporated herein, including logos, artwork, and other visual displays, that may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, service marks or trade names. We do not intend our use or display of other companies' trade names, service marks or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. All trademarks, service marks and trade names included or incorporated by reference into this Annual Report on Form 10-K and the documents filed as exhibits to the Annual Report on Form 10-K are the property of their respective owners.

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 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, non-viral therapeutic, 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 therapy, non-viral therapeutic, and other biological 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. VY7523, our anti-tau antibody candidate, is in early-stage clinical trials, and all of our other 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 we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, any of which could prevent us from commercializing our current and future product candidates on a timely basis, if at all.
- 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, substantially all of our revenue has been derived from our ongoing collaborations and licensing agreements with Neurocrine, Novartis, and Alexion and from our prior collaborations with Sanofi Genzyme Corporation, AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company. If any ongoing or future collaboration, option and license, or license agreements were to be terminated, our business financial condition, results of operations and prospects could be harmed.
- Our gene therapies, non-viral therapeutics, and other therapeutic modalities 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 gene therapy product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our gene therapy 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 whose mission is to leverage the power of human genetics to modify the course of and ultimately cure neurological diseases. Our pipeline includes programs for Alzheimer's disease, or AD; Friedreich's ataxia, or FA; Parkinson's disease; and multiple other diseases of the central nervous system, or CNS. Many of our programs are derived from our TRACER™ (Tropism Redirection of AAV by Cell-type-specific Expression of RNA) adeno-associated virus, or AAV, capsid discovery platform, which we have used to generate novel capsids, or TRACER Capsids, and identify associated receptors to potentially enable high brain penetration with genetic medicines following intravenous, or IV, dosing. Some of our programs are wholly-owned, and some are advancing with licensees and collaborators including Alexion, AstraZeneca Rare Disease, or Alexion; Novartis Pharma AG, or Novartis; and Neurocrine Biosciences, Inc., or Neurocrine.

We are advancing our own proprietary pipeline of drug candidates for neurological diseases, with a focus on AD, and particularly on tau, which we view as a critically important AD target. Our wholly-owned prioritized pipeline includes two tau targeting programs: VY7523 (which we formerly referred to as VY-TAU01), an anti-tau antibody for AD, and VY1706, a tau silencing gene therapy for AD. VY7523 is currently in a Phase 1, multiple ascending dose, or MAD, clinical trial in early AD patients, from which we expect initial tau positron emission tomography, or PET, imaging data in the second half of 2026. The murine version of VY7523 reduced tau spread by more than 70% in preclinical studies. VY7523 demonstrated an acceptable safety, tolerability, and immunogenicity profile as well as expected pharmacokinetic results in a Phase 1, single ascending dose, or SAD, clinical trial in healthy volunteers. No serious adverse events, or SAEs, severe adverse events, or infusion reactions were reported, and the cerebrospinal fluid, or CSF, -to-serum ratio was 0.3%. VY1706 is advancing towards anticipated submission of an investigational new drug, or IND, application in 2026. VY1706 was selected as the development candidate for the tau silencing gene therapy program in November 2024. In a non-human primate, or NHP, study, a single 1.3E13 vector genomes per kilogram, or vg/kg, dose of VY1706 delivered intravenously resulted in reductions in tau mRNA levels of 50% to 73% across the cerebral cortex, including in areas of the brain where tau accumulates during the progression of AD. Our proprietary pipeline also includes early research initiatives to develop a vectorized anti-amyloid antibody for AD and a vectorized superoxide dismutase 1, or SOD1, knockdown gene therapy for SOD1 amyotrophic lateral sclerosis, or ALS.

We are also working with our collaboration partners on multiple programs. We are advancing seven gene therapy programs with Neurocrine. Development candidates were selected for three of these programs in 2024, resulting in milestone payments to us. We expect that Neurocrine will submit IND filings in 2025 for the two most advanced of these programs, a glucosylceramidase beta 1, or GBA1, gene therapy program for Parkinson's disease and other GBA1-mediated diseases, and a frataxin, or FXN, gene therapy program for FA, or the FA Program. These two programs are particularly significant to us for two reasons: the subsequent clinical trials of these programs have the potential to establish human proof-of-concept for the TRACER Capsids, and we have the option to opt-in on co-development and co-commercialization in the United States for both products. In addition to the Neurocrine collaborations, we have partnered with Novartis on TRACER Capsid-based gene therapies for spinal muscular atrophy and Huntington's disease. We have also licensed capsids to Novartis for three undisclosed CNS targets and to Alexion for one undisclosed rare neurological disease target. In total, these partnerships have delivered more than $500.0 million in non-dilutive funding to us to date, including upfront fees, development milestone payments, option exercise fees, license fees, and research and development expense reimbursement. Looking forward, we have the potential to earn up to $8.2 billion in milestone payments across our partnered portfolio, including $2.9 billion in potential development milestone payments, as well as additional royalties.

All of the gene therapies in our wholly-owned and collaborative pipeline leverage TRACER. TRACER is a broadly applicable, RNA-based screening platform that enables rapid discovery of AAV capsids with robust penetration of the blood-brain barrier, or BBB, and enhanced CNS tropism in multiple species, including NHPs. We are also developing a second non-viral therapeutics platform focused on non-viral receptor-mediated transport across the BBB.

Vision, Mission, and Strategy

Our vision is a world in which transformative treatments and cures are available to the millions afflicted with neurological diseases. Our mission is to create disease-modifying neurogenetic medicines by identifying validated targets, advancing multiple therapeutic modalities, and delivering them to the right areas within the central nervous system.

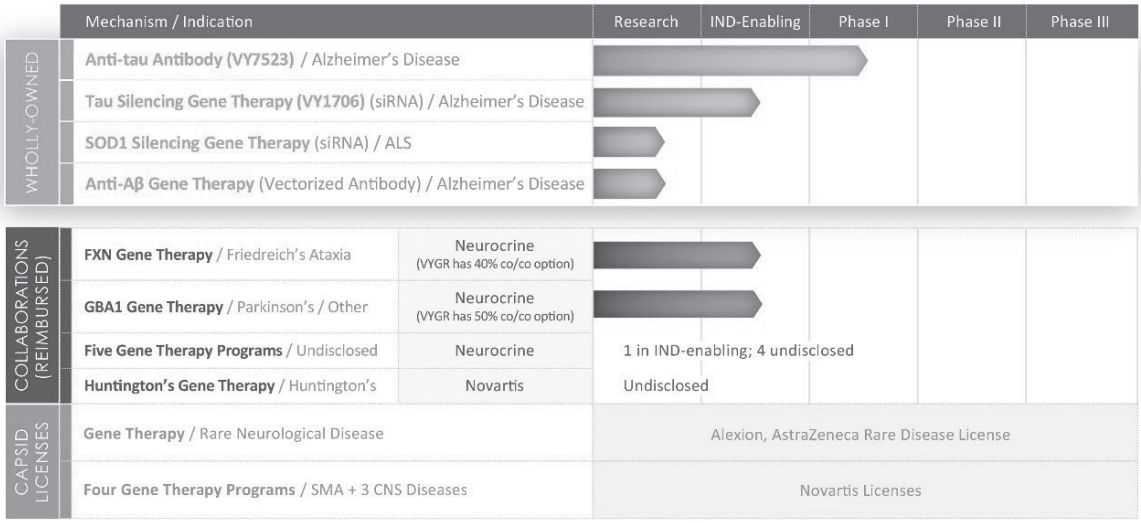
Our strategy is to leverage our expertise in BBB crossing and neuropharmacology, which we consider our key competitive advantages, to address the delivery hurdles that have constrained the neurology discipline. Our approach to leveraging genetics in the treatment of neurological diseases is centered on identifying and prioritizing programs for CNS diseases with:

- high unmet need,
- genetic targets validated by clinical or biological evidence,
- an efficient path to establish human proof-of-biology leveraging biomarkers,
- evidence of compelling preclinical pharmacology, and
- commercial potential.

We seek to select and advance the optimal modality to treat each disease. This may include enzymes, antibodies, or oligonucleotides, which may be enhanced for BBB penetration by vectorization within a TRACER Capsid or, as the non-viral therapeutics platform matures, combination with a non-viral BBB shuttle. Ultimately, our goal is to either halt or slow disease progression or reduce symptom severity and therefore provide clinically meaningful impact to patients.

Overview of Our Pipeline

Our pipeline of programs is summarized in the table below:



Our Platforms

We have expertise in both viral and non-viral approaches to targeting therapeutics to the brain.

Viral Delivery

Our TRACER Capsid discovery platform is a broadly applicable, RNA-based screening platform that enables rapid discovery of AAV capsids with robust penetration of the BBB-and enhanced CNS tropism observed in multiple animal species, including NHPs. TRACER allows us to identify proprietary AAV capsids, the outer viral protein shells that enclose genetic material that makes up the vector payload. TRACER facilitates the selection of AAV capsids with enhanced tissue delivery characteristics, such as more effective delivery across the BBB and cell-specific transduction. We believe that these TRACER Capsids have the potential to significantly enhance the activity and safety of our single dose gene therapy product candidates, which we expect to be delivered with a single systemic IV infusion, as compared with conventional capsids, which often require delivery via more invasive procedures. We have leveraged the TRACER discovery platform to generate multiple families of TRACER Capsids with robust CNS tropism following IV delivery. We have presented data at scientific conferences demonstrating strong transduction to multiple areas within the brain and activity across multiple animal species. We have entered into agreements with collaboration partners and licensees including Neurocrine, Novartis, and Alexion to provide access our TRACER Capsids for the development and commercialization of AAV gene therapy candidates in specified indications.

Monoclonal Antibodies and Non-Viral Delivery

We have additional expertise in the discovery and development of monoclonal antibodies as well as in receptor-mediated non-viral delivery to the CNS.

We have discovered multiple antibodies as part of the anti-tau antibody program and other research programs. Some of these programs have been advanced in a vectorized setting, such as our anti-amyloid program, while others have been advanced in a non-vectorized setting, such as the anti-tau antibody program.

Separately, we have identified receptors for some of our TRACER Capsids and are conducting experiments to evaluate the potential to leverage these receptors to shuttle non-viral genetic medicines across the BBB. Our non-viral therapeutics platform is initially focused on the receptor Alkaline Phosphatase (ALPL, formerly called Receptor X), a highly conserved cell surface receptor expressed at the BBB that our scientists identified as responsible for mediating enhanced brain tropism of one family of TRACER Capsids.

Wholly-Owned Programs

Anti-Tau Antibody (VY7523) and Tau Silencing Gene Therapy (VY1706) for the Treatment of Alzheimer's Disease

Disease Overview

Alzheimer's disease is a progressive neurodegenerative disease estimated to affect 7 million people in the United States and up to 416 million people globally. The disease causes memory loss and may escalate to decreased independence, communication challenges, behavioral disorders such as paranoia and anxiety, and lack of physical control. In 2023, the total cost of caring for people living with Alzheimer's and other dementias in the U.S. was estimated at $345 billion.

Our Focus on Tau

We view tau as a critically important target in the progression of AD. The spread of pathological tau as identified via tau PET imaging correlates closely to AD progression as measured by Braak clinical/pathologic staging. Further, recent third-party data have established that both an antibody and an antisense oligonucleotide knockdown approach can decrease accumulation of tau in the brain and potentially impact cognition.

Our Treatment Approach: VY7523 (Anti-Tau Antibody)

VY7523 is an IV-administered, recombinant, humanized IgG4 monoclonal antibody developed to inhibit the spread of pathological tau, which is closely correlated with disease progression and cognitive decline in AD. We selected VY7523 as our lead humanized anti-tau antibody candidate to advance against AD, choosing it from a pool of more than 700 anti-tau antibodies. This selection was based on empirical preclinical data regarding the ability to inhibit the spread of pathological tau in a mouse model, as detailed below. We believe VY7523 is differentiated from other anti-tau antibodies based on selectivity for pathological tau and the epitope, the part of a foreign protein or antigen that is capable of generating an immune response, it targets, which is located in the C-terminal rather than the N-terminal, mid-domain, or microtubule binding region of the tau protein.

Preclinical Studies

Our proprietary anti-tau antibodies have shown 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 (greater than 70%) reduction of induced tau pathology. In March 2024, we presented data at the Alzheimer's and Parkinson's Diseases, or AD/PD, 2024 Conference demonstrating VY7523 was well-tolerated, and its serum pharmacokinetic profile was as expected in an NHP study. In September 2024, at the Wells Fargo 2024 Healthcare Conference, we presented head-to-head preclinical data for a murine surrogate of VY7523 vs. murine surrogates of other anti-tau antibodies. The data demonstrated that the murine surrogate of VY7523 (C-terminal directed) achieved significant reduction in spread of human pathological tau in the P301S mouse seeding model, as did the murine surrogate of bepranemab (mid-domain directed). No significant reduction was seen for murine surrogates of two N-terminal directed antibodies we evaluated that previously had failed their primary endpoints in clinical trials. We expect to present additional data on these findings at AD/PD 2025 Conference.

Program Status

We conducted a randomized, double-blind, placebo-controlled SAD trial to evaluate the safety, tolerability, and pharmacokinetics of single IV doses of VY7523 in 48 healthy male and female volunteers. This trial was conducted at a single site between May 2024 and February 2025. The primary objective of the trial was to characterize the safety and tolerability of VY7523 in healthy adult participants, and the secondary objectives were to characterize the pharmacokinetics of VY7523 in serum and CSF following single, escalating IV doses and to evaluate the immunogenicity of single, escalating IV doses of VY7523. The primary endpoints for the trial were incidence of treatment-emergent adverse events and clinically relevant changes from baseline in vital signs, electrocardiograms, or ECGs, and clinical laboratory parameters. The secondary endpoints for the trial were various serum pharmacokinetic parameters, CSF concentrations of VY7523, and incidence, level, and characterization of treatment-emergent anti-drug antibodies, or ADAs. VY7523 was generally well tolerated across all six ascending dose cohorts, meeting the primary objective of the trial, with no SAEs, severe adverse events, or infusion reactions reported. The most frequently reported adverse events were pruritus/itchy skin and scratching, headache, and chest pain. Secondary objectives of the trial were also met. Serum concentrations increased in a dose-proportionate manner, and the CSF-to-serum ratio was 0.3%, consistent with other monoclonal antibodies approved for the treatment of AD. We expect to present additional data on the SAD trial at an upcoming scientific conference.

In February 2025, Voyager initiated a MAD trial of VY7523. The MAD study is a randomized, double-blind, placebo-controlled trial to evaluate VY7523 in 52 patients with early AD (mild cognitive impairment due to AD or mild AD). This trial will be conducted at multiple clinical trial sites in the U.S. and Canada. The primary objective is to characterize the safety and tolerability of VY7523 in participants with early AD, and the secondary objectives are to characterize the pharmacokinetics of VY7523 in serum and determine CSF concentrations following multiple IV doses, to evaluate the ability of VY7523 to prevent the spread of pathological tau, and to evaluate the immunogenicity of multiple, escalating IV doses of VY7523. The primary endpoints for the trial are incidence of treatment-emergent adverse events and clinically significant changes from baseline in vital signs, ECGs, and clinical and laboratory parameters. The secondary endpoints for the trial are serum VY7523 concentrations at specified timepoints, various serum pharmacokinetic parameters, CSF concentrations of VY7523, changes to baseline measurements of pathological tau by tau PET imaging, and incidence and level of treatment emergent ADAs. Initial tau PET imaging data are expected in the second half of 2026. Additional secondary endpoints include immunogenicity and pharmacokinetic parameters.

Our Treatment Approach: VY1706 (Tau Silencing Gene Therapy)

VY1706 is a gene therapy that leverages an intravenously delivered TRACER Capsid containing a vectorized siRNA, specifically targeting tau mRNA.

Preclinical Studies

In March 2024, we presented data at the AD/PD 2024 Conference demonstrating that a single IV administration of our tau silencing gene therapy in mice expressing human tau resulted in broad AAV distribution across multiple brain regions and dose-dependent reductions in tau mRNA levels of up to 90%, which were associated with robust reductions in human tau protein levels across the brain. In an NHP study, a single IV 1.3E13 vg/kg dose of VY1706 resulted in reductions in tau mRNA levels of 50% to 73% across the cerebral cortex, including in areas of the brain where tau accumulates during progression of AD. We expect to present additional data on these findings at AD/PD 2025.

Program Status

In November 2024, we nominated VY1706 as the development candidate for the tau gene silencing gene therapy program. We expect to file an IND for VY1706 in 2026.

SOD1 Silencing Gene Therapy Program for the Treatment of ALS

Our SOD1 silencing gene therapy program is in preclinical development. We are no longer advancing VY9323, previously our lead development candidate for the program, in light of emerging three-month NHP data from a good laboratory practice toxicology study suggesting that a different payload would be necessary to achieve the desired product profile for the program. We are currently assessing alternate payloads for the program. We anticipate that the program could combine the same intravenously-delivered TRACER Capsid utilized by VY9323 with an alternate SOD1 silencing payload.

Vectorized Anti-Amyloid Antibody Early Research Program for the Treatment of AD

In August 2023, we announced an early research initiative investigating a gene therapy targeting anti-amyloid for the treatment of AD. The program combines a vectorized anti-amyloid antibody with an intravenously delivered TRACER Capsid.

Collaboration Programs

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 5,000 patients living with the disease in the United States. While one treatment for Friedreich's ataxia has recently been approved by the FDA, we believe 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, and our collaboration partner Neurocrine, 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 IV 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 NHPs 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 NHPs 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

Under the collaboration and license agreement with Neurocrine entered into in January 2019, or the 2019 Neurocrine Collaboration Agreement, we are developing VY-FXN01 for the treatment of Friedreich's ataxia. VY-FXN01 is currently in preclinical development. In February 2024, the Joint Steering Committee ("JSC") with Neurocrine selected a development candidate combining an FXN gene replacement payload with a TRACER Capsid for the FA Program. We expect that Neurocrine will file an IND in 2025.

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, affecting 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, which 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 IV 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 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. At the AD/PD 2023 Conference, we presented new data from additional mouse efficacy studies showing that three potential development candidates each demonstrated significant improvement in several efficacy biomarkers. We presented data at the ASGCT 2023 Meeting summarizing the mouse findings and additional data from an NHP study showing that the administration of a reporter transgene via a single, IV dose using two novel BBB-penetrant AAV capsids demonstrated substantially improved biodistribution and gene expression compared to conventional AAV9 in the putamen and substantia nigra, two areas of the brain that are affected in Parkinson's disease.

Program Status

Under the collaboration and license agreement with Neurocrine entered into in January 2023, or 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, or the GBA1 Program. The GBA1 Program is currently in preclinical development. In April 2024, the Joint Steering Committee with Neurocrine selected a development candidate for the GBA1 Program. We expect that Neurocrine will file an IND in 2025.

HD Program (2023 Novartis Collaboration Agreement)

Disease Overview

Huntington's disease is a fatal, inherited neurodegenerative disease that results in the progressive decline of motor and cognitive functions and a range of behavioral and psychiatric disturbances. Huntington's disease is caused by mutations in the huntingtin, or HTT, gene. Huntington's disease is an autosomal dominant disorder, which means that an individual is at risk of inheriting the disease if only one parent is affected. While the exact function of the HTT gene in healthy individuals is unknown, it is essential for normal development before birth. Mutations in the HTT gene ultimately lead to the production of abnormal intracellular huntingtin protein aggregates and expansions in the gene in neurons that may cause neuronal cell death.

Program Status

On December 28, 2023, we entered into a license and collaboration agreement with Novartis, or the 2023 Novartis Collaboration Agreement. Under the 2023 Novartis Collaboration Agreement, we and Novartis have agreed to collaborate to develop AAV gene therapy products and product candidates intended for the treatment of Huntington's disease, which we refer to as the Novartis HD Program. The Novartis HD Program is currently in preclinical development. From and after the first IND application filing for the Novartis HD Program, we and Novartis have agreed that Novartis will assume sole responsibility for the development and commercialization of gene therapy products and

product candidates under the Novartis HD Program, including all further preclinical and clinical development and any commercialization of the Novartis HD Program products and product candidates.

Collaboration Programs and Licensing Agreements

2023 Novartis Collaboration Agreement

On December 28, 2023, or the 2023 Novartis Collaboration Agreement Effective Date, we entered into the 2023 Novartis Collaboration Agreement, with Novartis to (a) provide rights to Novartis with respect to certain TRACER Capsids for use in the research, development, and commercialization by Novartis of AAV gene therapy products and product candidates, comprising such TRACER Capsids and payloads intended for the treatment of spinal muscular atrophy, or the Novartis SMA Program, and (b) collaborate to develop AAV gene therapy products and product candidates under the Novartis HD Program, in each case, leveraging TRACER Capsids and other intellectual property controlled by us.

Novartis SMA Program and Novartis HD Program Licenses

Under the terms of the 2023 Novartis Collaboration Agreement, we granted to Novartis and its affiliates:

- a non-exclusive, non-transferable, non-sublicensable (except in limited circumstances for contractors), worldwide, royalty-free right and license under any patents or know-how controlled by us and related to the TRACER Capsids to evaluate the same for use in the development of a product or product candidate under the Novartis SMA Program, or a Novartis SMA Program Product, comprising such a TRACER Capsid and a payload selected by Novartis during the period beginning on the 2023 Novartis Collaboration Agreement Effective Date and ending on the third anniversary of the 2023 Novartis Collaboration Agreement Effective Date;

- an exclusive (even as to us), sublicensable, non-transferable, worldwide, royalty-bearing right and license under any patents or know-how controlled by us and relating to the selected TRACER Capsids to exploit the same as incorporated into a Novartis SMA Program Product for all human and veterinary diagnostic, prophylactic and therapeutic uses during the 2023 Novartis Collaboration Term (as defined below); and

- an exclusive (even as to us), non-transferable, sublicensable, worldwide, royalty-bearing right and license under any patents and know-how controlled by us and relating to the development of a product or product candidate under the Novartis HD Program, or a Novartis HD Program Product to exploit the same for all human and veterinary diagnostic, prophylactic and therapeutic uses during the 2023 Novartis Collaboration Term.

Governance

We and Novartis have agreed to manage the Novartis HD Program through a Joint Steering Committee until dissolved after the first IND application filing for a Novartis HD Program Product. We and Novartis have further agreed that day-to-day activities of both the Novartis SMA Program and the Novartis HD Program shall be managed through designees from each of us and Novartis, acting as alliance managers.

Development, Regulatory Approval, Commercialization and Diligence.

Under the 2023 Novartis Collaboration Agreement, Novartis is solely responsible for, and has sole decision-making authority with respect to, at its own expense, the exploitation of a Novartis SMA Program Product.

With respect to the Novartis HD Program, the parties have agreed to conduct research and pre-clinical development of Novartis HD Program Products pursuant to a research plan, with Novartis reimbursing us for our activities thereunder in accordance with the agreed-to budget. From and after the first IND application filing for the Novartis HD Program, the parties have agreed that Novartis will assume sole responsibility for the development and

commercialization of Novartis HD Program Products, including all further preclinical and clinical development and any commercialization of the Novartis HD Program products and product candidates.

With respect to each of the Novartis SMA Program Products and Novartis HD Program Products, Novartis is obligated to use commercially reasonable efforts to develop and obtain regulatory approval for at least one of each such product in the United States and in certain other international markets specified in the 2023 Novartis Collaboration Agreement.

Intellectual Property

Under the terms of the 2023 Novartis Collaboration 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 2023 Novartis Collaboration Agreement Effective Date, or invented, authored, discovered, developed, created or acquired solely by or on behalf of such party after the 2023 Novartis Collaboration Effective Date outside of its activities under the 2023 Novartis Collaboration Agreement.

We and Novartis have further agreed that all know-how created by either or both parties in the performance of the activities as undertaken pursuant to the performance of the Novartis HD Program plan or in the course of development, manufacture and commercialization of Novartis HD Program Products and all patent rights covering such know-how, or collectively, the 2023 Novartis Arising IP, is to be owned as follows: (i) we solely own all 2023 Novartis Arising IP comprised of know-how or other intellectual property rights related to any TRACER Capsid, including the use or manufacture of any TRACER Capsid, and that is created jointly by our representatives and representatives of Novartis or created solely by representatives of Novartis through the use of our confidential information; and (b) with respect to all other 2023 Novartis Arising IP, (i) we solely own all such 2023 Novartis Arising IP created solely by our representatives, (ii) Novartis solely owns all such 2023 Novartis Arising IP created solely by Novartis representatives; and (iii) the parties jointly own all such 2023 Novartis Arising IP created jointly by representatives of both Novartis and us.

Exclusivity

Subject to certain limitations and exceptions, we have agreed during the 2023 Novartis Collaboration Term not to (a) conduct any wholly-owned program or program on behalf of a third party that is directed to the development or commercialization of any capsids for use in any therapeutic product containing a capsid in combination with a payload designed to have therapeutic effect on the gene agreed between the parties as the target of the Novartis SMA Program when packaged into a capsid and delivered to the appropriate cells; (b) develop or commercialize any competing Novartis HD Program Product intended to have a therapeutic effect on genes agreed between the parties as the targets of the Novartis HD Program; or (c) grant any third party any right, license, option, covenant not to assert or similar right, under any patents or know-how controlled by us or our affiliates (excluding an acquiring entity) as of the 2023 Novartis Collaboration Agreement Effective Date or during the 2023 Novartis Collaboration Term, that would enable a third party to do any of the foregoing.

Termination

Unless earlier terminated, with respect to any licensed product(s) under the 2023 Novartis Collaboration Agreement, on a country-by-country basis, the 2023 Novartis Collaboration Agreement expires upon the expiration of the last-to-expire royalty term with respect to such licensed product in such country in the territory, or the 2023 Novartis Collaboration Term. Subject to a cure period, either party may terminate the 2023 Novartis Collaboration 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 2023 Novartis Collaboration Agreement, in whole or in part, subject to specified conditions, for our insolvency, for 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 2023 Novartis Collaboration Agreement, in whole or in part, for any or no reason upon ninety days' written notice to us. In the event that Novartis has the right to terminate the 2023 Novartis Collaboration Agreement as a result of an uncured material breach by us that materially impairs the ability of Novartis to exploit one or more licensed products, Novartis may, in lieu of such termination, elect for the 2023 Novartis Collaboration Agreement to remain in full force and effect, and all milestone payments and royalties that would have otherwise been payable by Novartis under such licenses had the 2023 Novartis Collaboration Agreement not been breached would be substantially reduced.

Financial Terms

Under the 2023 Novartis Collaboration Agreement, Novartis paid us an upfront payment of $80.0 million. We are eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of $200.0 million for the Novartis SMA Program and up to an aggregate of $225.0 million for the Novartis HD Program, in each case for the first corresponding product to achieve the corresponding milestone. We are also eligible to receive (a) specified sales milestone payments of up to an aggregate of $400.0 million for the Novartis SMA Program and up to an aggregate of $375.0 million for the Novartis HD Program and (b) tiered, escalating royalties in the high single-digit to low double-digit percentages of annual net sales of the Novartis SMA Program Products and the Novartis HD Program Products. The royalties are subject to potential customary reductions, including patent claim expiration, payments for certain third-party licenses, and biosimilar market penetration, subject to specified limits.

2022 Novartis Option and License Agreement

Summary of Agreement

On March 4, 2022, or the 2022 Novartis Option and License Effective Date, we entered into an option and license agreement with Novartis, or the 2022 Novartis Option and License Agreement. Pursuant to the 2022 Novartis Option and License Agreement, we granted Novartis options, or the Novartis License Options, to license TRACER Capsids, or the Novartis Licensed Capsids, for exclusive use in programs targeting three specified genes, or the Initial Novartis Targets, to develop and commercialize AAV gene therapy candidates comprised of Novartis Licensed Capsids and payloads directed to such targets, or the Novartis Initial Licensed Products. Effective as of March 1, 2023, Novartis exercised its Novartis License Options to license TRACER Capsids for use in gene therapy programs against two undisclosed programs targeting specified genes, or the Initial Novartis Targets. Upon Novartis' exercise of the two Novartis License Options for Initial Novartis Targets, we granted 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 Novartis Initial Licensed Products. We also agreed to provide certain additional know-how to enable Novartis to exploit the Novartis Licensed Capsid and a payload directed to the applicable Initial Novartis Target for use in an Initial Novartis Licensed Product. Novartis elected not to license a capsid for one Initial Novartis Target 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 third Initial Novartis Target terminated, and all capsid rights with respect to that Initial Novartis Target returned to us.

On September 3, 2024, we entered into an amendment, or the Novartis Amendment, to the 2022 Novartis Option and License Agreement. Pursuant to the Novartis Amendment, we agreed to amend the 2022 Novartis Option and License Agreement to incorporate the grant to Novartis of a direct license, or the Novartis Direct License, to a TRACER Capsid, or the Novartis Direct Licensed Capsid, for exclusive use with a certain gene, or the Novartis Direct License

Target, to develop and commercialize the Novartis Direct Licensed Capsid as incorporated into AAV gene therapy candidates comprised of the Novartis Direct Licensed Capsid and a payload directed to the Novartis Direct License Target, or Novartis Direct Licensed Products. We refer to (a) the two Initial Novartis Targets for which Novartis has exercised its Novartis License Options and the Novartis Direct License Target collectively as Novartis Licensed Targets, and (b) the Novartis Initial Licensed Products and Novartis Direct Licensed Products collectively as Novartis Licensed Products. As a result of the Novartis Amendment, the Novartis Direct License Target is now deemed a Licensed Target under the 2022 Novartis Option and License Agreement, as such term is defined therein, and the Novartis Direct License is subject to all other terms and conditions applicable to other licenses granted to Novartis under the 2022 Novartis Option and License Agreement. In connection with the Novartis Amendment, the parties acknowledged that Novartis' prior rights to exercise options for any initial targets and additional targets as described in the 2022 Novartis Option and License Agreement, other than those that had previously been exercised, had expired as of the effective date of the Novartis Amendment.

Research Term

During the period commencing on September 3, 2024 and ending on September 3, 2026 with respect to the Novartis Direct License Target, or the Novartis Research Term, on a target-by-target basis, we have granted Novartis a non-exclusive research license to evaluate our TRACER Capsids for potential use, in combination with a payload directed the applicable Novartis Direct License Target. 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.

Novartis may, during the applicable Novartis Research Term, conduct additional evaluation of our capsid candidates and has the right to substitute any other TRACER Capsid for a Novartis Licensed Capsid.

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 the parties.

Development, Regulatory Approval, and Commercialization

Under the 2022 Novartis Option and License Agreement, Novartis is solely responsible for, and has sole decision-making authority with respect to, development and commercialization of the Novartis Licensed Products. Novartis is required to use commercially reasonable efforts to develop and obtain regulatory approval for at least one Novartis Licensed Product for each Novartis Licensed Target 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 we refer to as 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, 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, in addition to its 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 a payload directed to the corresponding Novartis Licensed Target.

Financial

Under the terms of the 2022 Novartis Option and License Agreement, Novartis paid us an upfront payment of $54.0 million. Effective as of March 1, 2023, Novartis exercised its Novartis License Options to license TRACER Capsids for use in gene therapy programs against two undisclosed Initial Novartis Targets. With Novartis' option exercise on two Initial Novartis Targets, we received a $25.0 million option exercise payment in April 2023. Novartis paid us a one-time fee of $15.0 million in consideration for the rights granted under the Novartis Amendment, which we received in October 2024. We are eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of $125.0 million for the first Novartis Initial Licensed Product for each Initial Novartis Target for which a Novartis License Option has been exercised to achieve the corresponding milestone. Additionally, we are eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of $130.0 million for the first Novartis Direct Licensed Product to achieve the corresponding milestone. On a Novartis Licensed Product-by-Novartis Licensed Product basis, we are also eligible to receive (a) specified sales milestone payments of up to an aggregate of $175.0 million per Novartis Licensed Product and (b) tiered, escalating royalties in the mid- to high-single-digit percentages based on annual net sales of each Novartis Licensed Product incorporating the Novartis Licensed Capsids. The Novartis Licensed Targets are distinct from targets in our wholly-owned and partnered pipeline.

Intellectual Property

Under the terms of the 2022 Novartis Option and License Agreement, each party owns the entire right, title, and interest in and to all patents or know-how controlled by such party and existing as of or before the 2022 Novartis Option and License Effective Date, or invented, developed, created, generated or acquired solely by or on behalf of such party after the 2022 Novartis Option and License 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 2022 Novartis Option and License Agreement and in the course of the parties' activities under the 2022 Novartis Option and License 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, not to conduct any internal program or program on behalf of a third party that is directed to the development or commercialization of any of 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 Novartis Licensed Targets; and (b) not to grant any third party or affiliate any right or license under our patents to exploit any Novartis Licensed Capsid for any of the Novartis Licensed Targets.

Termination

Unless earlier terminated, the 2022 Novartis Option and License 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 2022 Novartis Option and License Agreement, in whole or in part, subject to specified conditions, in the event of the other party's uncured material breach. Novartis may also terminate the 2022 Novartis Option and License 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 2022 Novartis Option and License Agreement, in whole or in part, for any or no reason upon ninety days' written notice to us.

Upon certain terminations for cause by Novartis, the licenses granted by us to Novartis under the 2022 Novartis Option and License Agreement shall become irrevocable and perpetual, and all milestone payments and royalties that would have otherwise been payable by Novartis under such licenses had the 2022 Novartis Option and License Agreement remained in effect would be substantially reduced.

2023 Neurocrine Collaboration Agreement

Summary of Agreement

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

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 Joint Steering Committee 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. With the exception of one preclinical study where we agreed to share costs, Neurocrine has agreed to be responsible for all costs we incur in conducting preclinical development activities for each 2023 Neurocrine Program, in accordance with JSC-agreed upon workplans and budgets. 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 our 50% share of profits. The 2023 Co-Co Trigger Event is the date on which we receive topline data from the first clinical trial for a product candidate being developed for Parkinson's disease pursuant to the GBA1 Program or if none, then another indication under the GBA1 Program.

Governance

Our research and development activities under the 2023 Neurocrine 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, (i) 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 (ii) 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. We agreed to forfeit certain milestones and royalties on net sales in the United States if we exercise the 2023 Co-Co Option. The JSC's selection of the lead development candidate for the GBA1 Program in April 2024 triggered a $3.0 million milestone payment, which we received in May 2024. Additionally, the JSC's selection of the development candidate for a 2023 Discovery Program in September 2024 triggered a $3.0 million milestone payment, which we received in October 2024.

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 (x) 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, (y) ten years from the first commercial sale of the 2023 Collaboration Product in such country and (z) 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 Neurocrine Arising IP, is to be owned as follows: (a) we solely own all 2023 Neurocrine Arising IP created jointly by representatives of us and Neurocrine that constitutes capsid know-how and capsid patent rights, and 2023 Neurocrine 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 Neurocrine Arising IP, (i) we solely own all such 2023 Neurocrine Arising IP created solely by our representatives, (ii) Neurocrine solely owns all such 2023 Neurocrine Arising IP created solely by Neurocrine representatives; and (iii) the parties jointly own all such 2023 Neurocrine Arising IP created jointly by representatives of both Neurocrine and us. 2023 Neurocrine 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 (x) 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 (y) 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 (i) is substantially irreversible or not monitorable in

patients or (ii) 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.

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 four collaboration programs, which we refer to collectively as the 2019 Neurocrine Programs: the NBIb-1817 (VY-AADC) program for the treatment of Parkinson's disease, or the VY-AADC Program; the FA Program; and other undisclosed programs, or the 2019 Discovery Programs. 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 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. 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.

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 of the 2019 Discovery Programs, on a worldwide basis. Licenses related to the VY-AADC Program terminated in August 2021.

In connection with the June 2019 termination of the collaboration agreement with Sanofi Genzyme Corporation, we gained 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 the JSC, we have operational responsibility, subject to certain exceptions, for the conduct of each 2019 Neurocrine Program prior to the occurrence of a specified event for each 2019 Neurocrine Program, or a 2019 Transition Event, 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 2019 Transition Event for each 2019 Neurocrine Program, 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 the FA Program, we were granted the option, or the 2019 Co-Co Option, to co-develop and co-commercialize the FA Program upon the occurrence of a specified event, or the 2019 Co-Co Trigger Event. We agreed, were we to exercise the 2019 Co-Co Option, to enter into a cost- and profit-sharing arrangement with Neurocrine, or the 2019 Co-Co Agreement, and (a) jointly develop and commercialize 2019 Collaboration Products for the FA 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 2019 Co-Co Agreement. The 2019 Transition Events are (x) 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 (y) 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 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 the 2019 Co-Co Option would be allocated 60% to Neurocrine and 40% to us for a 2019 Collaboration Product. The parties agreed that the 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 the FA Program, subject to specified exceptions, (i) Neurocrine has the right to resolve such matter prior to our exercise of the 2019 Co-Co Option with regard to an applicable 2019 Co-Co Product or if the 2019 Co-Co Option expires or goes unexercised and (ii) following the timely exercise by us of the 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 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. We completed the nomination process with Neurocrine, and the JSC approved the two targets for development under the 2019 Discovery Programs. The two targets are currently under development.

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 the 2019 Co-Co Agreement, if applicable.

Financial Terms

Under the terms of the 2019 Neurocrine Collaboration Agreement, Neurocrine 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 FA Program of up to $195.0 million, and (b) 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. The JSC's selection of the development candidate for the FA Program in February 2024 triggered a $5.0 million milestone payment, which we received in March 2024. We are no

longer eligible to receive milestone or royalty payments for the VY-AADC Program in light of the partial termination of the 2019 Neurocrine Collaboration Agreement with respect to the VY-AADC Program.

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 FA Program, from the low-teens to high-teens and high-single digits to mid-teens, respectively; and (b) 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.

Alexion Option and License Agreement (Formerly Pfizer Option and License Agreement)

Summary of Agreement

We are party to an option and license agreement, or the Alexion Agreement, with Alexion. We initially entered into the Alexion Agreement with Pfizer, Inc., or Pfizer, on October 1, 2021, or the Alexion Agreement Effective Date. However, Alexion (via Alexion Pharma International Operations Limited, or APIO) later acquired all of Pfizer's rights under the Alexion Agreement and became the successor-in-interest to Pfizer thereunder effective upon the closing of a definitive purchase and license agreement between Pfizer and Alexion on September 20, 2023. APIO subsequently assigned the Alexion Agreement to its affiliate AstraZeneca Ireland Limited, or AstraZeneca. Neither the acquisition by Alexion nor the subsequent assignment from APIO to AstraZeneca impacted the material terms of the Alexion Agreement. Pursuant to the Alexion Agreement, we have granted Alexion an exclusive, worldwide license, with the right to sublicense, under certain of our intellectual property, the rights to develop and commercialize AAV gene therapy products for the potential treatment of a rare neurological disease comprised of a TRACER Capsid, or the Alexion Licensed Capsid, and a specified transgene, or the Alexion Transgene. We refer to such AAV gene therapy products as Alexion Licensed CNS Products.

Prior to Alexion's acquisition of all of Pfizer's rights under the Alexion Agreement, we had granted Pfizer the right to exercise up to two options to license TRACER Capsids to develop and commercialize certain AAV gene therapy candidates comprised of a TRACER Capsid and a specified transgene. Effective as of September 30, 2022, Pfizer exercised its option with respect to a TRACER Capsid for a specified transgene for potential treatment of a rare neurological disease. All of Pfizer's rights in connection with such option exercise were transferred to Alexion as discussed above. Pfizer did not exercise its option with respect to any TRACER Capsid for a specified transgene for the potential treatment of a cardiovascular disease. As result, all rights to any TRACER Capsids for that cardiovascular disease reverted to us in accordance with the terms of the Alexion Agreement.

Research Term

The Alexion Agreement provides for a research term commencing on the Alexion Agreement Effective Date and expiring on April 1, 2025 (which was initially set to expire on September 30, 2024, but was extended until such date pursuant to an amendment to the Alexion Agreement effective as of September 30, 2024), or the Alexion Research Term. Until the expiration of the Alexion Research Term, while we are not obligated to conduct additional research activities to identify additional TRACER Capsids that may be useful for AAV gene therapies for the treatment of rare neurological diseases, we have agreed to continue to disclose to Alexion, on a rolling basis, the performance characteristics identified for all such TRACER Capsids, if and when available. Alexion may, during the Alexion Research Term, conduct additional evaluations of such TRACER Capsids and has the right to substitute any other TRACER Capsid for the TRACER Capsid that is currently licensed under the Alexion Agreement.

Development, Regulatory Approval and Commercialization

Under the Alexion Agreement, Alexion is solely responsible for, and has sole decision-making authority with respect to, development and commercialization of the Alexion Licensed CNS Products. Alexion is required to use commercially reasonable efforts to develop and obtain regulatory approval for at least one Alexion Licensed CNS Product 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 we refer to as an Alexion Major Market Country, subject to certain limitations. Alexion is also required to use commercially reasonable efforts to commercialize each Alexion Licensed CNS Product in the United States and at least one Alexion Major Market Country where Alexion or its designated affiliates or sublicensees has received regulatory approval for such Alexion Licensed CNS Product, subject to certain limitations.

Intellectual Property

Under the terms of the Alexion Agreement, each of the parties 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 Alexion 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 Alexion Agreement and in the course of our and Alexion's activities under the Alexion Agreement will follow inventorship under U.S. patent law. Subject to certain limitations and exceptions, we have agreed (a) during the Alexion 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 Alexion Transgene, in any indication for therapeutic, diagnostic and prophylactic human and veterinary use; and (b) not to grant any third party or affiliate any right or license under our patents to exploit any licensed capsid in combination with any Alexion Transgene.

Financial

Prior to Pfizer's transfer of its rights under the Alexion Agreement to Alexion, Pfizer paid us an upfront payment of $30.0 million in October 2021, and an additional fee of $10.0 million in connection with its exercise of an option. We are eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of $115.0 million for the first corresponding Alexion Licensed CNS Product to achieve the corresponding milestone. On an Alexion Licensed CNS Product-by-Alexion Licensed CNS Product basis, we are also eligible to receive (a) specified sales milestone payments of up to an aggregate of $175.0 million per Alexion Licensed CNS Product and (b) tiered, escalating royalties in the mid- to high-single-digit percentages of annual net sales of each Alexion 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 Alexion Agreement expires on the expiration of the last-to-expire royalty term with respect to all Alexion Licensed CNS Products in all countries. Subject to a cure period, either party may terminate the Alexion Agreement, in whole or in part, subject to specified conditions, in the event of the other party's uncured material breach. Alexion may also terminate the Alexion 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 noncompliance with certain anti-bribery or anti-corruption covenants. Alexion may also terminate the Alexion Agreement, in whole or in part, for any or no reason upon ninety days' written notice to us.

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

License Agreement with Touchlight IP Limited

On November 3, 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.

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 certain 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 certain 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 expect that our TRACER discovery platform, non-viral therapeutics platform, and preclinical programs will compete with a variety of therapies in development, including:

- Our anti-tau antibody and tau silencing gene therapy programs for AD will potentially compete with tau antibodies being developed by Lundbeck LLC, Merck & Co., Inc. in collaboration with Teijin Limited, Eisai Co., Ltd., Janssen Pharmaceuticals, Inc., UCB S.A., Bristol-Myers Squibb Company in collaboration with Prothena Corporation plc, along with several other companies, as well as an antisense oligonucleotide program being developed by Ionis Pharmaceuticals, Inc. in collaboration with Biogen Inc.;

- Our program for a monogenic form of ALS will potentially compete with tofersen being developed by Biogen Inc., in collaboration with Ionis Pharmaceuticals, Inc., and gene therapies being developed by Novartis Gene Therapies, Inc. and uniQure, Inc.;

- 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., Sangamo Therapeutics, Inc., and Shape Therapeutics Inc; and

- Our non-viral therapeutics platform will potentially compete with a variety of companies developing non-viral shuttles for the delivery of genetic medicines to the CNS, including: ABL Bio, Inc. in collaboration with Sanofi S.A., Aliada Therapeutics, Inc. (acquired by AbbVie Inc.), Arrowhead Pharmaceuticals, Inc. in collaboration with Sarepta Therapeutics, Inc., BioArctic AB in collaboration with Eisai Co., Ltd., Denali Therapeutics Inc., F. Hoffmann-La Roche Ltd, JCR Pharmaceuticals Co., Ltd., and Souffle Therapeutics, Inc.

We are aware of several companies focused on developing AAV gene therapies in various indications, including Abeona Therapeutics Inc., Adverum Biotechnologies, Inc., Akouos, Inc. (acquired by Eli Lilly and Company, or Eli Lilly), Alcyone Therapeutics, Inc., Amicus Therapeutics, Inc., Asklepios BioPharmaceutical, Inc. (acquired by Bayer AG), Astellas Gene Therapies, Inc., Beacon Therapeutics Holdings Limited, Biogen, Inc., BioMarin Pharmaceutical Inc., Encoded Therapeutics, Inc., GenSight Biologics S.A., LEXEO Therapeutics, Inc., LogicBio Therapeutics, Inc. (acquired by AstraZeneca), MeiraGTx Ltd., Neurogene Inc., Novartis Gene Therapies, Inc. (formerly AveXis, Inc.), Passage Bio, Inc., Pfizer Inc., Prevail Therapeutics Inc. (acquired by Eli Lilly), REGENXBio Inc., Sarepta Therapeutics, Inc., Solid Biosciences Inc., Spark Therapeutics, Inc. (acquired by Genentech, Inc.), Taysha Gene

Therapies, Inc. and uniQure, Inc., 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.

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, non-viral therapeutic, and other biological 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 AAV gene therapy trials we have developed a proprietary HEK 293 transient transfection manufacturing process that is scalable for large scale AAV manufacturing – both for preclinical research activities and clinical and commercial manufacturing. We continuously innovate and develop advanced manufacturing technologies to enable high yields and product quality, and we manufacture preclinical AAV material for large animal studies at our onsite, state-of-the-art chemistry, manufacturing, and controls, or CMC, development facility. Our current AAV gene therapy manufacturing process is being transferred to our contract manufacturing organizations to enable clinical current good manufacturing practice, or cGMP manufacturing.

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 cGMP manufacturing capabilities. The use of contract 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 neurogenetic medicines and 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 know-how; and operate without infringing the valid and 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 and patents 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 using or manufacturing the same.

We own at least 421 pending patent applications and at least 113 patents have issued in the United States and foreign jurisdictions. We co-own at least 33 pending patent applications and at least 13 patents have issued from these co-owned families in the United States and foreign jurisdictions. At least nine 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 17 patents have issued to our licensors which have granted us exclusive license rights to the technology. To date, at least 63 patents have issued to our licensors which have granted us non-exclusive license rights to the technology with at least 43 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 product candidates and business. We seek U.S. and international patent protection for a variety of technologies, including: AAV-based biological products and constructs, antibodies, non-viral therapeutic modalities, methods of delivering said AAV-based biological products and constructs, antibodies and non-viral modalities, 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 know-how and 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

Tauopathies

We own 10 pending patent families directed to antibodies to tau and vectorized forms thereof with 43 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, 2043, 2044, and 2045 all of which are subject to possible patent term extensions.

We own five pending patent families to RNA inhibitors for treating tauopathies with seven pending non-provisional patent applications and three pending provisional applications. Patents that grant from this family are generally expected to commence expiration in 2043, 2044, and 2045, subject to possible patent term extensions.

Friedreich's Ataxia

We own six pending patent families with two granted patent and 25 patent applications and we co-own one pending patent family with seven patent applications and 1 granted patent 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, 2040, and 2044, all of which are subject to possible patent term extensions.

GBA1 Gene Therapy

We own eight pending patent families with 27 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, 2042, 2043, 2044, and 2045, subject to possible patent term extensions.

Huntington's Disease

We own four pending patent families with 10 granted patents and 21 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 and 2040, all of which are subject to possible patent term extensions.

Parkinson's Disease

We own three pending patent families with nine issued patents and at least 21 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, 2038, and 2039, subject to possible patent term extensions.

ALS

We own seven pending patent families and have 22 issued patents and 31 patent applications directed to targeting SOD1 for the treatment of ALS. We co-own an eighth patent family with six 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. Patents that grant from these patent families are generally expected to commence expiration in 2035, with some applications expiring in 2038, 2039, 2040, 2042, and 2044, all of which are 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 one granted patent and 12 pending applications, which are generally expected to commence expiration in 2039 and 2041, respectively, subject to possible patent term extensions.

We also own 11 pending patent families comprising 87 pending U.S. and foreign applications and one granted U.S. patent, as well as one pending provisional application directed to capsid variants identified using the TRACER discovery platform showing improved properties over their wild-type AAV counterparts. Patents that grant from these patent families and pending provisional applications are generally expected to commence expiration in 2041, 2042, 2043, 2044, and 2045, subject to possible patent term extensions.

We own at least 12 patent families comprising 20 pending non-provisional applications and we co-own three 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, 2043, 2044, and 2045, subject to possible patent term extensions.

We also own one patent family pending in the United States and foreign jurisdictions directed to capsid variants generated using other methodologies. In this pending patent family, there are four granted patents and 9 pending patent applications. Patents that grant from this patent family are generally expected to commence expiration in 2038, subject to possible patent term extensions. We also co-own two patent families directed to other capsid variants. In these two pending patent families there are three 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.

Non-Viral Therapeutics

We own one pending patent family with six pending non-provisional patent applications directed to ligands to capsid receptors. Patents that grant from these pending non-provisional applications are generally expected to commence expiration in 2044, 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.

Regulatable Expression

We own one pending patent family with three pending patent application 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.

Vector and Genome Engineering

We own three patent families with 52 issued patents (including 15 patents in European countries) and 36 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 10 granted patents and at least 55 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 ten granted patents and eight 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.

Other

We own two pending patent families with four pending patent applications 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 and 2043, subject to possible patent term extensions.

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.

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 four 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. Two of the four families of patents and applications are exclusively licensed and comprise 3 granted patents and seven applications in the United States and other territories. Two of the four families of patents and applications are non-exclusively licensed and comprise three granted patents in the United States. Patents that grant from these patent families are generally expected to expire between 2025 and 2036, subject to possible patent term extensions.

We have exclusively licensed one family of patents and patent applications directed to AAV capsids from the University of Massachusetts. In this pending patent family, there are 14 granted patents and two pending patent applications. Patents that grant from this patent family are generally expected to commence expiration in 2031, 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 52 granted patents and one pending application. 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 eight granted patents and one pending application. 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 at least 41 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 have registered trademarks and service marks or pending trademarks and service mark applications in the United States and a number of other countries for the in the marks VOYAGER and VOYAGER (with design elements), which we presently use or may use in connection with our pharmaceutical research and development services and our biological preparations for gene therapy for the treatment of various diseases.

We also own registrations in the United States and 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.”

In connection with the ongoing development and advancement of our products and services in the U.S. and in various international jurisdictions, we routinely seek to create protection for our marks and enhance their value by pursuing trademarks and service marks where available and when appropriate. We plan to register trademarks in connection with our biological products.

Protection of Confidential Information, Know-how and Trade Secrets

We may rely, in some circumstances, on confidential information, know-how and 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, know-how 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 confidential information, know-how and 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 and antibody 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 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;

- payment of user application and program fees pursuant to the Prescription Drug User Fee Act, or PDUFA;

- FDA review and approval of the BLA, authorizing licensure of the biological product for marketing of the product in the US for one or more indications; 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. 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 new drug application, or 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 or studies and places the trial on a clinical hold. The FDA may also place a hold or partial hold on a clinical study based on chemistry, manufacturing, and controls issues involving the investigational product. In either 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.

An IRB representing each institution participating in the clinical trial must also 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 Health and Human Services, or HHS, and FDA regulations, must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects before the study can commence at the institution 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 monitoring committee, or DMC. This group provides an independent recommendation 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 DMC maintains access. Suspension or termination of development during any phase of a clinical trial can occur if the DMC recommends stopping a trial due to safety or efficacy.

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 trial, 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.

Phase 2 clinical trials are generally conducted in a 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 3 clinical trials proceed if the prior clinical trials demonstrate that the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken in the proposed patient population to provide evidence of clinical efficacy and safety. A well-controlled, statistically robust Phase 3 clinical trial is designed to deliver the data that regulatory authorities will use to decide whether or not to approve the product candidate, 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 or rare patient population.

In December 2022, with the passage of the Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan, or DAP, 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, action 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 June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on diversity, equity and inclusion programs, the FDA removed this draft guidance from its website. The implications of this action are not yet known.

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 post-marketing studies or clinical trials, may be conducted after initial marketing approval. These trials are used to either gain additional experience from the treatment of a larger number of patients in the intended treatment group or to evaluate a specific outcome of interest (safety or efficacy). In certain instances, the FDA may mandate the performance of post-marketing studies or 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 post-marketing studies or clinical trials could result in withdrawal of FDA approval for products.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance is adopted from the International Council for Harmonisation's recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

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. The Final Rule also implemented reporting requirements for results of clinical trials listed on clinicaltrials.gov. Although the FDA has historically not enforced these reporting requirements, the FDA has, as of December 19, 2024, issued six notices of non-compliance, thereby signaling the government's willingness to begin enforcing these requirements against non-compliant clinical trial sponsors. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov 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. Violations may also result in injunctions and/or criminal prosecution or disqualification from federal grants.

Clinical Studies Outside of the United States in Support of FDA Approval

In connection with the clinical development of our programs, we may conduct trials at sites outside of the United States. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. 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 NDA or a BLA. Specifically, the studies must be conducted in accordance with GCPs, 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. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

The acceptance by the FDA of study data from clinical trials conducted outside the United States in support of United States approval may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted.

Interactions with the FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, a sponsor is given the opportunity to meet with the FDA at certain points in the clinical development program. There are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-NDA meetings as well as end of phase meetings such as end of Phase 2, or EOP2, meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product. A Type D meeting is focused on a narrow set of issues and should not require input from more than three disciplines or divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges early in the development of an investigational product.

At the conclusion of these meetings, the FDA will typically provide its responses to questions posed by the sponsor regarding the clinical development program. The FDA will not indicate whether an NDA or BLA will be approved, but it will provide guidance to the sponsor on various questions, including whether an application should be submitted in the first place on the basis of the studies and data proposed by the sponsor. The agency may also generally express support for the sponsor's approach in the clinical development program but indicate that questions concerning whether the data support approval will be subject to review by the agency following its acceptance for filing of the NDA or BLA. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Gene Therapy Products

We expect that the procedures and standards applied to gene therapy products will be applied to any gene therapy 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. 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 Therapeutic Products, or OTP. The FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The NIH, including the Novel and Exceptional Technology and Research Advisory Committee, or 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 a draft guidance issued in November 2024 to address frequently asked questions surrounding the development of cellular and gene therapy products. Although the FDA has indicated that these and other guidance documents it previously issued are not legally binding, the guidance documents provide the FDA's current thinking on, 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 has typically recommended that sponsors continue to monitor participants for potential gene therapy-related adverse events for up to a five-year period. The FDA recommends that these long-term follow-up studies include, at a minimum, five years of annual physical examinations followed by annual queries, either in-person or by phone or written questionnaire, for the remaining observation period.

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 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.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless granted a deferral or waiver. The sponsor must submit an initial pediatric study plan within 60 days of an EOP2 meeting or as may be agreed between the sponsor and the FDA. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. A waiver may be granted when the disease or condition does not occur in pediatrics. Unless otherwise required by regulation, the pediatric data requirements generally do not apply to products with orphan designation although FDA has taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

Submission of a BLA to the FDA

FDA approval is required before any new biologic product can be marketed in the United States. Thus, assuming successful completion of all required preclinical and human testing in accordance with all applicable regulatory requirements, detailed product information is submitted to the FDA in the form of a BLA. 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. For federal fiscal year 2025, the application user fee is $4,310,002 for an application requiring clinical data, and the sponsor of a licensed BLA is subject to an annual program fee, which for fiscal year 2025 is $403,889.

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 the 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 seeks to meet these timelines for review of an application but its ability to do so may be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. For example, during the past decade, the U.S. government has shut down several times and certain regulatory agencies,

including the FDA, have had to furlough critical employees and stop critical activities, including the review of both NDAs and BLAs when funding from PDUFA fee payments was exhausted.

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.

Moreover, the FDA will review a sponsor's financial relationship with the principal investigators who conducted the clinical trials in support of the BLA or NDA. Depending on the level of that compensation and any other financial interest a principal investigator may have in a sponsor, the sponsor may be required to report these relationships to the FDA. The FDA will then evaluate that financial relationship and determine whether it creates a conflict of interest or otherwise affects the interpretation of the trial, or the integrity of the data generated at the principal investigator's clinical trial site. If so, the FDA may exclude data from the clinical trial site in connection with its determination of the approvability of the application for the investigational product.

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. To reach this determination, the FDA must determine that the investigational product is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety, purity and potency in the BLA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks.

The FDA typically requires a robust safety database and 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. The FDA issued draft guidance in September 2023 that outlines considerations for relying on confirmatory evidence in lieu of a second clinical trial to demonstrate efficacy.

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. 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. During the product approval process, the FDA also will determine whether a REMS is necessary to assure the safe use of the 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.

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 post-marketing studies or 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 studies, clinical 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

Biologic 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 this legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products.

In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls

for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product.

Further, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws. The Prescription Drug Marketing Act, or PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. In November 2013, the federal Drug Supply Chain Security Act became effective in the United States, mandating an industry-wide, electronic, interoperable system to trace prescription drugs through the pharmaceutical distribution supply chain with a ten-year phase-in process. Manufacturers were required by November 2023 to have such systems and processes in place. So as not to disrupt supply chains, the FDA has granted certain exemptions from enhanced drug distribution security requirements for eligible trading partners for particular periods of time.

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, this designation enables a company to petition FDA to initiate review of sections of a NDA or BLA 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, 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. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. 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 studies or clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of all promotional materials.

With the passage of FDORA, 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 and to submit progress reports on its post-approval studies to FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval study of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner or the Commissioner's designee and a written appeal, among other things.

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The agency indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidance relating to accelerated approval. This guidance describes FDA's views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While this guidance is currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

- *Regenerative Medicine Advanced Therapy (RMAT) designation*. With the 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 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 as stipulated in the ODD. 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 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 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 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 therapy in the same indication as defined by the FDA.

In September 2021, the Court of Appeals for the 11th Circuit, in *Catalyst Pharms, Inc. v. Becerra*, or *Catalyst*, held that, for the purpose of determining the scope of orphan drug 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 approved "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 the Catalyst 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 is approved. More recently however, on February 14, 2025, a federal district court in Washington, DC fully embraced the reasoning of the Catalyst decision in another decision challenging the scope of orphan drug exclusivity. The implications of this decision, and its impact on the FDA's implementation of the Orphan Drug Act, are unclear at this point.

Priority Review Vouchers

A priority review voucher, or 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 NDAs 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.

Under the statutory sunset provisions for the Rare Pediatric Disease PRV Program, the FDA was authorized to award a PRV for an approved rare pediatric disease product application if the rare pediatric disease designation was granted by December 20, 2024, and the BLA or NDA for that product is approved before September 30, 2026. This program was not reauthorized by the Congress in 2024, although there appears to be Congressional support for doing so during the next Congressional session.

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 both biosimilar products and 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.

The BPCIA also includes provisions to protect reference products that have patent protection. The biosimilar product sponsor and reference product sponsor may exchange certain patent and product information for the purpose of determining whether there should be a legal patent challenge. Based on the outcome of negotiations surrounding the exchanged information, the reference product sponsor may bring a patent infringement suit and injunction proceedings against the biosimilar product sponsor. The biosimilar applicant may also be able to bring an action for declaratory judgment concerning the patent.

The FDA maintains a publicly-available online database of licensed biological products, which is commonly referred to as the "Purple Book." The Purple Book lists product names, dates of licensure, and applicable periods of exclusivity. Further, the reference product sponsor must provide patent information and patent expiry dates to FDA following the exchange of patent information between biosimilar and reference product sponsors. This information is then published in the Purple Book.

There have been recent government proposals to reduce the 12-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.

Pediatric Exclusivity

Pediatric exclusivity is a type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of exclusivity. For biologic products, the six-month period may be attached to any existing regulatory exclusivities but not to any patent terms. The conditions for pediatric exclusivity include the FDA's determination that information relating to the use of a new product in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric clinical trials, and the sponsor agreeing to perform, and reporting on, the requested clinical trials within the statutory timeframe. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data does not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity that cover the product are extended by six months.

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, or FCPA, 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.

On February 10, 2025, President Trump issued an Executive Order directing the Attorney General to review the guidelines and policies governing FCPA investigations and enforcement actions. Per the Executive Order, this review will result in new DOJ FCPA guidelines intended to enhance American economic competitiveness and to safeguard national security interests. During the 180-day review period, any new FCPA investigations and enforcement actions are to be suspended absent authorization from the Attorney General, and all existing FCPA investigations and enforcement actions will be reviewed. Additionally, after the Attorney General issues revised guidelines, the Executive Order directs her to assess whether "remedial measures" related to past FCPA actions are warranted. The implications of this action are not clear.

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.

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 June 17, 2021, the United States Supreme Court dismissed a challenge to the ACA after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA.

During the first Trump Administration, the Congress and administration sought to overturn the ACA and related measures. Shortly after taking office in January 2025, President Trump revoked numerous executive orders issued by President Biden, including at least two executive orders (e.g., EO 14009, Strengthening Medicaid and the Affordable Care Act, and EO 14070, Continuing to Strengthen Americans' Access to Affordable, Quality Health Coverage) that were designed to further implement the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Pharmaceutical Price Reform

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been 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 addition, 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. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Five states (Colorado, Florida, Maine, New Hampshire and New Mexico) have submitted Section 804 Importation Program proposals to the FDA, and, on January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. That state now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.

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 also 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. The Inflation Reduction Act of 2022, or IRA, further delayed implementation of this rule to January 1, 2032.

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. In addition, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs. 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.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, the HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On January 17, 2025, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations. Thereafter, following the change in administrations, CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program. The second cycle of negotiations with participating drug companies is expected to occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

On June 6, 2023, Merck & Co. filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, the Pharmaceutical Research and Manufacturers of America, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. Litigation involving these and other provisions of the IRA will continue with unpredictable and uncertain results.

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. This may be increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval.

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 in these countries.

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 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 93,449 square feet located in Lexington, MA. Our lease in Cambridge expires in 2026 and our lease in Lexington expires in 2031. We have subleased our office and laboratory space in Cambridge to a third party.

Employees and Human Capital Resources

As of December 31, 2024, we employed 172 full-time employees in the United States, including 139 in research and development positions and 33 in general and administrative positions. Approximately 57 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, 2024.

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 biotechnology 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 a net loss of $65.0 million, net income of $132.3 million, and a net loss of $46.4 million for the years ended December 31, 2024, 2023, and 2022, respectively. As of December 31, 2024, we had an accumulated deficit of $326.2 million.

We historically have financed our operations primarily through private placements of our redeemable convertible preferred stock, public offerings and private placements 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, and Novartis Pharma AG, or Novartis; our option and license agreement, or the Alexion Agreement, with Alexion, AstraZeneca Rare Disease, or Alexion; and our option and license agreement, or the 2022 Novartis Option and License Agreement, with 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 and non-viral therapeutics platforms, selecting product programs, conducting research and development, including preclinical and clinical 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 clinical trials in connection with our anti-tau antibody program;
- continue investing in our proprietary antibody program, non-viral therapeutics platform, gene therapy and vectorized antibody platforms and programs, and other research and development initiatives;
- continue investing in and supporting TRACER™ (Tropism Redirection of AAV by Cell-type-specific Expression of RNA), our proprietary discovery platform to facilitate the selection of adeno-associated

virus, or AAV, capsids, which we refer to as TRACER Capsids, and our investment to discover TRACER Capsids with broad tropism in CNS and other tissues with cell-specific transduction properties for particular therapeutic applications;

- increase our investment in the discovery and development of modalities for receptor-mediated non-viral delivery of therapeutic payloads to the CNS;

- conduct joint research and development under our strategic collaborations for the research, development, and commercialization of certain of our pipeline programs, including our Friedreich's ataxia program, or the FA Program, pursuant to our collaboration and license agreement with Neurocrine entered into in January 2019, or the 2019 Neurocrine Collaboration Agreement, our glucosylceramidase beta 1, or GBA1, gene therapy program for Parkinson's disease and other GBA1-mediated diseases, or the GBA1 Program, pursuant to our collaboration and license agreement with Neurocrine entered into in January 2023, or the 2023 Neurocrine Collaboration Agreement, and our Huntington's disease program, or the Novartis HD Program, pursuant to our license and collaboration agreement with Novartis entered into in December 2023, or the 2023 Novartis 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 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;

- increase our clinical trial insurance coverage as we expand our clinical trials and increase our product liability insurance once we engage in 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 U.S. Food and Drug Administration, or 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 development;
- 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 viable treatment options;
- 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, 2024, our cash, cash equivalents, and marketable securities were $332.4 million. Based upon our current operating plan, we expect that our existing cash, cash equivalents, and marketable securities at December 31, 2024 along with amounts expected to be received as reimbursement for development costs under our collaboration and license agreements with Neurocrine and Novartis, and interest income, to be sufficient to meet our planned operating expenses and capital expenditure requirements into mid-2027.

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; including our clinical trials to evaluate VY7523;

- 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 arrangements we may enter into in the future, including any research and development costs for which we are responsible, future additional obligations that we may be committed to in connection with these agreements, and our receipt of any expense reimbursements, 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 license agreement we entered into with Touchlight IP Limited, or Touchlight, in November 2022, 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. 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 or option and license 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.

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 partners, Neurocrine and Novartis, and licensees for the reimbursement of certain research and development expenses, potential option exercises, the achievement of specified regulatory and commercial milestones, and royalty payments under the 2019 Neurocrine Collaboration Agreement, the 2023 Neurocrine Collaboration Agreement, and the 2023 Novartis Collaboration Agreement and the amounts we are entitled to receive from our licensees Alexion 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 early 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. VY7523, our anti-tau antibody candidate, is in early-stage clinical trials, and. all of our other 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 conducted such as those put on 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 as we advance our programs

into the clinical stage. 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, non-viral therapeutic, 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.

Our future success depends on our successful development of AAV gene therapy and other biological therapy product candidates, including our anti-tau antibody candidate and non-viral therapeutic product candidates. VY7523, our anti-tau antibody candidate, is in early-stage clinical trials. Each of the other 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. For example, we are no longer advancing VY9323, formerly the lead development candidate for our superoxide dismutase 1, or SOD1, silencing program for amyotrophic lateral sclerosis, or ALS, as a development candidate and are assessing alternate payloads for the program based on three-month data from a non-human primate good laboratory practice, or GLP, toxicology study suggesting that a different payload would be necessary to achieve the desired product profile for the program. We also may experience unanticipated problems or delays in expanding our manufacturing capacity or outsourcing manufacturing activities to contract manufacturers.

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. In Europe, a similarly limited number of AAV gene therapy products have been granted marketing authorization.

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 of gene therapies 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 biological, gene therapy, and other non-viral therapeutic 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.

U.S. regulations require each clinical trial site's institutional review board, or IRB, to 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 proprietary antibody and 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.

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.

Any inability to receive timely, actionable feedback from regulatory authorities could also delay or otherwise hinder our development efforts. 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 have conducted, and may in the future conduct, clinical trials for product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.

We have conducted, and may in the future choose to conduct, one or more of our clinical trials outside the United States. To date, we have conducted clinical trials in the United States and Canada. 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 clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where the foreign trial data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the trial satisfies certain conditions. 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 are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial we conduct 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. Even if the FDA accepted such data, it could require us to modify our planned clinical trials to receive clearance to initiate such trials in the United States or to continue such trials once initiated.

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

- foreign regulatory requirements, differences in healthcare services, and differences in cultural customs 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 or early-stage clinical development. We may encounter substantial delays or difficulties in commencement, enrollment or completion of our preclinical studies or clinical trials, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, any of 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. VY7523, our anti-tau antibody candidate, is currently in early-stage clinical trials, and all of our other 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, capsid discovery, and other studies require certain NHPs that are customarily imported from outside the United States. Our inability to obtain access to a sufficient supply of these NHPs in a timely manner or at all may impair or delay our ability to complete preclinical studies to support capsid discovery efforts or IND applications or similar applications in other jurisdictions. We have previously encountered, and may encounter in the future, delays in obtaining a sufficient supply of such NHPs due to governmental or regulatory actions that result in importation restrictions in the United States or exportation restrictions in the country of origin. At times when the NHP supply in the United States has been constrained, we have conducted NHP studies at contract research facilities outside of the United States. When utilizing such facilities, we are required to observe export control regulations for the shipment of product candidates and their component materials and import control regulations for the shipment of samples to us for evaluation and storage. We may be required to incur delays or expenses in order to conduct our NHP studies in compliance with these regulations, and we may be subject to additional penalties, delays, or expenses if we fail to achieve compliance.

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 successfully 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, or DAP, 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, action 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 DAPs. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission

of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. The implications of this action are not yet known.

Similarly, the regulatory landscape related to clinical trials in the European Union, or 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. Similarly, there may be delays or difficulties in our initiation of future clinical trials. For example, we no longer expect to file an IND or Canadian clinical trial application for VY9323, formerly the lead development candidate for our SOD1 silencing program for ALS, and are assessing alternate payloads for the program based on three-month data from a non-human primate GLP toxicology study suggesting that a different payload would be necessary to achieve the desired product profile for the program.

We also have very limited historical experience with clinical trials as a company. 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 proprietary antibody, AAV gene therapy, and non-viral therapeutic 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, Canada, 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 SAE, 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 SAEs associated with the product candidate that are viewed to outweigh its potential benefits;

- occurrence of SAEs 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 to an HEK 293-based production system from 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, safety warnings or contraindications;
- 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 sued or otherwise become party to dispute proceedings; or
- experience damage to our reputation.

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.

Our proprietary antibodies and gene therapy product candidates may cause an immunologic reaction, or an immune response against the relevant product candidate. Other potential side effects associated with our gene therapy product candidates could include 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. 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. 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 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 example, product candidates designed to "knock down" or reduce the expression of a gene or the production of its encoded protein could have effects on other parts of the body, or "off target" effects, that 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, the Court of Appeals for the 11th Circuit, in *Catalyst Pharms, Inc. v. Becerra*, or *Catalyst*, held that, for the purpose of determining the scope of orphan drug 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 approved "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 the *Catalyst* 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 is approved. More recently however, on February 14, 2025, a federal district court in Washington, DC fully embraced the reasoning of the Catalyst decision in another decision challenging the scope of orphan drug exclusivity. The implications of this decision, and its impact on the FDA's implementation of the Orphan Drug Act, are unclear at this point.

In addition, to obtain orphan drug designation in the European Union, we would need to demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized

in the European Union or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition. There is no assurance that we would be able to meet that standard for any of our product candidates. Further, if we do obtain orphan drug designation for a candidate product in the EU, we will not be able to maintain that designation if we are not able to show, to the satisfaction of the EU regulatory authorities, that the candidate product is of significant benefit to patients over available commercial products for the indication in the EU and any additional products that are ahead of our product candidate in clinical development for the indication.

A potential breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may 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.

Where appropriate, we may pursue approval from the FDA, EMA or comparable foreign regulatory authorities through the use of accelerated registration pathways. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, EMA or comparable regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA, EMA or such other regulatory authorities may seek to withdraw accelerated approval.

Where appropriate, we plan to pursue accelerated development strategies in areas of medical need. We may seek an accelerated approval pathway for one or more of our product candidates from the FDA, EMA or comparable foreign regulatory authorities. Under the accelerated approval provisions in the Federal Food, Drug, and Cosmetic Act, and the FDA's implementing regulations, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or

other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug or biologic over available therapy may not be a direct therapeutic advantage but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's or biologic's clinical benefit. If such post-approval studies fail to confirm the drug's or biologic's clinical benefit, the FDA may withdraw its approval of the product.

In addition, there can be no assurance that we will satisfy all FDA requirements, including new provisions, that govern accelerated approval. For example, with passage of the 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 and to submit progress reports on its post-approval studies to FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval study of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner or the Commissioner's designee and a written appeal, among other things. We will need to fully comply with these and other requirements in connection with the development and approval of any product candidate that qualifies for accelerated approval.

More recently, in March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The FDA indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidance relating to accelerated approval. This guidance describes FDA's views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While this guidance is currently only in draft form and will ultimately not be legally binding even when finalized, we will need to consider the FDA's guidance if we seek accelerated approval for any of our products in the future.

Prior to seeking accelerated approval, we will seek feedback from the FDA, EMA or comparable foreign regulatory authorities and will otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit a BLA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent feedback from the FDA, EMA or comparable foreign regulatory authorities, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so.

Furthermore, if we decide to submit an application for accelerated approval, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA, EMA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

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.

Further, the FDA may determine that we must provide additional evidence and data before approving a BLA or NDA for our candidate products. For example, the FDA reviews an application to determine whether there is "substantial evidence" to support a finding of effectiveness for the proposed product for its intended use(s). The FDA has interpreted this evidentiary standard to generally require at least two adequate and well-controlled clinical trials to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional confirmatory evidence may satisfy this standard. The FDA issued draft guidance in September 2023 that outlines considerations for relying on confirmatory evidence in lieu of a second clinical trial to demonstrate effectiveness. In the event that we submit a BLA or NDA on the basis of one clinical trial and confirmatory evidence, the FDA could determine that such information is not sufficient to support approval of the application and the agency could require us to conduct an additional trial in support of the BLA or NDA.

The FDA may also require that NDA or BLA submissions for our product candidates include pediatric data. Under the PREA, an NDA, BLA or supplement to an NDA or BLA for certain drugs and biological products must contain data to assess the safety and effectiveness of the drug or biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. Applicable legislation in the EU also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the European Medicines Agency, or EMA, or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we are seeking regulatory approval in the United States or the EU, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

Moreover, principal investigators for our future clinical trials may serve as scientific advisors or consultants to us and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing

applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

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 $4.3 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 post-marketing studies or 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, we could be adversely affected by several significant administrative law cases decided by the U.S. Supreme Court in 2024. In *Loper Bright Enterprises v. Raimondo*, for example, the Court overruled *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc*., which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U.S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act, or the APA. Additionally, in *Corner Post, Inc. v. Board of Governors of the Federal Reserve System*, the Court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, *Securities and Exchange Commission v. Jarkesy*, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations.

Further, our ability to develop and market new drug products may be impacted by litigation challenging the FDA's approval of another company's drug product. In April 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021, were arbitrary and capricious. In June 2024, the Supreme Court reversed that decision after unanimously finding that the plaintiffs (anti-abortion doctors and organizations) did not have standing to bring this legal action against the FDA. On October 11, 2024, the Attorneys General of three states (Missouri, Idaho and Kansas) filed an amended complaint in the district court in Texas challenging FDA's actions. On January 16, 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge. Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation.

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.

Disruptions in the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel or otherwise prevent new product candidates and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

In addition, disruptions may result from events similar to the COVID-19 pandemic. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

Further, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. There is also uncertainty as to how other measures being implemented by the Trump Administration across the government will impact our activities and those of the FDA and its operations. For example, the potential loss of FDA personnel could lead to further disruptions and delays in FDA review of our product candidates and FDA guidance regarding our or our collaborators' clinical development programs. Similarly, efforts by the new administration to substantially reduce research funding by the National Institutes of Health of medical research could have substantial direct or indirect impacts on our research activities.

Accordingly, if a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

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, non-viral therapeutics platform, product programs, product candidates and scientific expertise in the fields of proprietary antibodies, 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 their proprietary antibodies, AAV gene therapies, or non-viral therapeutics in various indications, as well as several companies addressing other methods for modifying genes and regulating gene expression. Any advances in antibody, gene therapy, or non-viral therapeutic 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, non-viral therapeutics platform, and clinical and preclinical programs will compete with a variety of therapies in development, including:

- Our anti-tau antibody and tau silencing gene therapy programs for AD will potentially compete with tau antibodies being developed by Lundbeck LLC, Merck & Co., Inc. in collaboration with Teijin Limited, Eisai Co., Ltd., Janssen Pharmaceuticals, Inc., UCB S.A., Bristol-Myers Squibb Company in collaboration with Prothena Corporation plc, along with 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 uniQure, Inc.; and

- 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., Sangamo Therapeutics, Inc., and Shape Therapeutics Inc.

- Our non-viral therapeutics platform will potential compete with a variety of companies developing non-viral shuttles for the delivery of genetic medicines to the CNS, including: ABL Bio, Inc. in collaboration with Sanofi S.A., Aliada Therapeutics, Inc. (acquired by AbbVie Inc.), Arrowhead Pharmaceuticals, Inc. in collaboration with Sarepta Therapeutics, Inc., BioArctic AB in collaboration with Eisai Co., Ltd., Denali Therapeutics Inc., F. Hoffmann-La Roche Ltd JCR Pharmaceuticals Co., Ltd., and Souffle Therapeutics, 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.

Even if our competitors are unsuccessful in developing and commercializing their product candidates, their preclinical and clinical findings may lead us to conclude that our own similar product candidates are unlikely to achieve the desired performance characteristics. As a result, we may modify our development plans for, or discontinue further research and development of, such product candidates. For example, several of our competitors are conducting clinical trials of anti-tau antisense oligonucleotide and antibody candidates with expected clinical data readouts in 2025 and 2026. It is possible that we will modify our development plans for, or discontinue further research and development of, VY7523 or VY1706, the lead development candidate for our tau gene silencing gene therapy program, if any of these clinical data readouts suggest that either candidate will likely fail to achieve the desired performance characteristics.

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, we could face heightened risks with respect to obtaining marketing authorization in the UK as a result of the withdrawal of the UK from the EU, commonly referred to as Brexit. The UK is no longer part of the European Single Market and EU Customs Union. As of January 1, 2025, the Medicines and Healthcare Products Regulatory Agency, or MHRA, is responsible for approving all medicinal products destined for the United Kingdom market (i.e., Great Britain and Northern Ireland). At the same time, a new international recognition procedure, or IRP, will apply, which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the EU/European Economic Area member states for approvals in

the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the United States). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the UK for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (including potentially reducing the duration of regulatory data protection and revising the eligibility for expedited pathways) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may however have a significant impact on the pharmaceutical industry and our business in the long term.

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, increasing interest rates, 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 rely on the reference product or sponsor's data, or the company does not 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, substantially all of our revenue has been derived from our ongoing collaborations and licensing agreements with Neurocrine, Novartis, and Alexion, and from our prior collaborations with Sanofi Genzyme, AbbVie Biotechnology Ltd and AbbVie Ireland Unlimited Company, or AbbVie. If any ongoing or future collaboration, option and license, or license agreements were to be terminated, our business financial condition, results of operations and prospects could be harmed.

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

Our ability to generate revenues from these arrangements will depend on our collaborators' success in performing the functions assigned to them in these arrangements. 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, on January 8, 2023, we entered into a second collaboration agreement, or the 2023 Neurocrine Collaboration Agreement, with Neurocrine 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 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, or the 2023 Discovery Programs, and, collectively with the GBA1 Program, the 2023 Neurocrine Programs. On December 28, 2023, we entered into the 2023 Novartis Collaboration Agreement to (a) provide rights to Novartis with respect to certain of our TRACER Capsids for use in the research, development, and commercialization by Novartis of AAV gene therapy products and product candidates, comprising such TRACER Capsids and payloads intended for the treatment of spinal muscular atrophy, or the Novartis SMA Program, and (b) collaborate to develop AAV gene therapy products and product candidates intended for the treatment of Huntington's disease under the Novartis HD Program, in each case, leveraging our TRACER Capsids and other intellectual property controlled by us.

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 proprietary antibody program and 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;

- in collaboration, licensing, and option arrangements where we have licensed intellectual property rights to collaborators, licensees, and optionees who have the right to control prosecution of the licensed intellectual property rights, disputes may arise with respect to the prosecution strategy for the relevant intellectual property rights, which may impair our ability to pursue our preferred prosecution strategy or achieve the desired protection from any relevant patents;

- 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 or Novartis, Neurocrine or Novartis 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 proprietary antibody program or gene therapy and vectorized antibody platforms and programs. 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 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, non-viral therapeutics, and other biological products 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, non-viral therapeutic, and other biological 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 AAV gene therapy manufacturing platform that is based on proprietary technology and provides a scalable process for preclinical and clinical AAV production. We are using a HEK 293 based transient transfection manufacturing process to support our preclinical research activities. As the field advances, we will continue to evaluate additional novel manufacturing technologies that may be suitable for future clinical and commercial manufacturing.

We presently contract with third parties for the manufacturing of our program materials for our proprietary antibody and gene therapy product candidates. We have also built an onsite, state-of-the-art process research and development facility to enable the manufacturing of preclinical AAV gene therapy vectors for large animal studies including IND enabling GLP toxicology materials. We do not currently have our own clinical or commercial scale manufacturing. The use of contract 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 clinical and commercial manufacturing, third parties with whom we currently work might need to increase their scale of production, or we may need to secure additional suppliers as part of our external manufacturing network. 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 and technology transfers with such sources, if necessary, would not result in significant delay or material additional costs. However, if a third-party manufacturer decided to not enter into a new contract with us for program materials or if they did not have the capacity to meet our needs for program materials, we may be required to contract with additional suppliers on terms which may be less favorable to us or would result in additional material 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 proprietary antibody and AAV product candidates. However, we are dependent on one third-party manufacturer to produce our AAV and one for the tau antibody clinical 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 AAV product candidates using a mammalian cell system. We are aware of third parties which also use this system 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 proprietary antibody program and our gene therapy, vectorized antibody, and non-viral therapeutics platforms and programs. Research programs to identify new product candidates require substantial technical, financial and human resources. Most of our product candidates are in preclinical development, and one is in early-stage clinical trials. Our current portfolio of product candidates is subject to change as we continue to conduct preclinical and clinical testing and to develop product candidates and prioritize or abandon product candidates based on

such results and other factors. For example, we are no longer advancing VY9323, formerly the lead development candidate for our SOD1 silencing program for ALS, as a development candidate and are assessing alternate payloads for the program based on three-month data from a non-human primate GLP toxicology study suggesting that a different payload would be necessary to achieve the desired product profile for the program. 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 programs, 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 licensing or collaboration 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 2032 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, in June 2021, the United States Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the statute. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

During the first Trump Administration, the Congress and administration sought to overturn the ACA and related measures. Shortly after taking office in January 2025, President Trump revoked numerous executive orders issued by President Biden, including at least two executive orders (e.g., EO 14009, Strengthening Medicaid and the Affordable Care Act, and EO 14070, Continuing to Strengthen Americans' Access to Affordable, Quality Health Coverage) where were designed to further implement the ACA. We anticipate similar efforts to undermine the ACA, and the accompanying uncertainty, for the foreseeable future.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

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 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, reduce the costs of pharmaceuticals under Medicare and Medicaid, and reform government program reimbursement methodologies for products.

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. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Five states (Colorado, Florida, Maine, New Hampshire and New Mexico) have submitted Section 804 Importation Program proposals to the FDA, and, on January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. That state now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.

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 rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed, and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. The Inflation Reduction Act of 2022, or IRA, further delayed implementation of this rule to January 1, 2032.

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. 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 IRA also established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs.

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.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, the HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On January 17, 2025, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations. Thereafter, following the change in administrations, CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater

transparency in the negotiation program. The second cycle of negotiations with participating drug companies is expected to occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

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 downward 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. This may be increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval.

In other countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. 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.

Our relationships with healthcare providers, physicians and third-party payors will be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription and use of our products and any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered products to report payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals; and

- analogous state and foreign laws and regulations, such as state anti-kickback, false claims, and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require product manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations or the operations of our present and future collaborators are found to be in violation of any of the laws described above or any government regulations that apply to us or them, we or they may be subject to penalties, including civil and criminal penalties, damages, fines, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our or their financial results. We are developing and implementing a corporate compliance program designed to ensure that we will market and sell any future products that we successfully develop from our product candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect us from governmental investigations or

other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Efforts to ensure that our business with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. For example, we are engaged in an ongoing effort to improve our healthcare compliance program and establish a more robust compliance infrastructure. We may fail to establish appropriate compliance measures, and even with a stronger program in place, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

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 also prohibited in other jurisdictions. The provision of benefits or advantages to physicians is governed by anti-bribery laws of European Union Member States and the UK Bribery Act 2010.

Payments made to physicians in certain European Union Member States must be publicly disclosed and 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. 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 to California, at least 18 other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. There are also states that are considering or have already passed comprehensive privacy laws that will go into effect in 2025 and beyond. There are also states that are specifically regulating health information that may affect our business. For example, Washington state recently passed a health privacy law that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. 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.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business.

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 Data Protection Act of 2018 applies to the processing of personal data that takes place in the UK 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 Securities and Exchange Commission, or SEC, should be viewed with caution. Further, the data and statistical information used in such reports, including estimates derived from them, may differ from information and estimates made by our competitors or from current or future studies conducted by independent sources.

The use of such data involves risks and uncertainties, and such data is subject to change based on various factors. Our estimates may prove to be incorrect, and new studies may change the estimated incidence or prevalence of

the diseases we seek to address. The number of patients with the diseases we are targeting in the United States, the European Union and elsewhere may turn out to be lower than expected or may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or access, all of which would harm our results of operations and our business.

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 achievement of milestones or metrics specified in the applicable development plan, as determined by the JSC, 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 the 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 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 our 50% 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 in Parkinson's disease 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 certain 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 gene therapy 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 proprietary antibody and 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 proprietary antibody and 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 gene therapy product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our gene therapy 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 recent 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/or 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 and biotechnology and biopharmaceutical companies in the gene therapy and non-viral therapeutic fields 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, particularly due to the competitive and rapidly-evolving gene therapy and non-viral therapeutic patent landscape. 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 impact the scope of our rights to the relevant intellectual property or technology, result in delays and increased costs associated with the resolution of the disagreements, result in termination of our access to such intellectual property, or increase our financial or other obligations to our licensors, licensees, or collaborators.

The agreements under which we currently in-license intellectual property or technology from, or out-license our intellectual property to, 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 result in delays and costs associated with the resolution of such disagreement, impact what we believe to be the scope of our or the third party's rights to the relevant intellectual property or technology, result in loss of access to a license or other rights that are necessary for developing, commercializing and protecting our platform technologies and products, result in allegations that we have failed to comply with our obligations under any licenses or related agreements, 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.

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 2024 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. Following Brexit, there have been changes associated with obtaining, defending, and enforcing intellectual property rights in the United Kingdom, including requirements for separate filings and registrations in the United Kingdom that may lead to increased costs and risks associated with obtaining or maintaining 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 subject matter eligibility, lack of novelty, obviousness, lack of written description, failure to enable third parties to practice the relevant invention, or double patenting, in particular, obviousness-type double patenting, which if successful, could result in a finding that the claims are invalid or the loss of patent term, including a patent term adjustment granted by the USPTO, if a terminal disclaimer is filed to obviate a finding of obviousness-type double patenting. 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. Touchlight had made us aware in early 2022 that it believed that some of 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 rights. 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 or other proprietary confidential information or know-how 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 increased pressure to invest 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 owned or 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. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. For example, the Supreme Court of the United States held in *Amgen v. Sanofi* (May 18, 2023) that a functionally claimed genus was invalid for failing to comply with the enablement requirement of the Patent Act of 1952. In addition, the Federal Circuit has recently issued several decisions involving the interaction of patent term adjustment, terminal disclaimers, and obviousness-type double patenting (*Allergan USA, Inc. v. MSN Laboratory Private Ltd*. (August 13, 2024); *In re: Cellect. LLC* (August 28, 2023)). The courts have also addressed issues pertaining to patenting genes or gene products. 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 gene therapy 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, an approved 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 antibody, gene therapy, or non-viral therapeutic 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, or result in issued patents with a scope of protection that could be designed around or circumvented by our competitors;

- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;

- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we may not develop additional proprietary technologies that are patentable;

- the patents of others may have an adverse effect on our business; and

- we may choose not to file a patent for certain inventions, trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

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

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

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

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

Our reliance on third parties requires us to share our trade secrets, confidential information and know-how, which increases the possibility that a competitor will discover them or that our trade secrets, confidential information and/or know-how 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 proprietary antibody program and gene therapy, vectorized antibody, and non-viral therapeutic platforms and programs, 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 and know-how increases the risk that such trade secrets and confidential information and know-how become known by our competitors, are inadvertently incorporated into the technology of others, are included in third-party patent or regulatory filings, 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 and know-how, our competitors may discover our trade secrets or know-how, either through breach of these agreements, independent development or publication of information including our trade secrets or know-how by third parties. A competitor's discovery of our trade secrets and/or know-how 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 January 2024, we completed a private placement of 2,145,002 shares of our common stock to Novartis and an underwritten public offering of 7,777,778 shares of our common stock and pre-funded warrants to purchase up to 3,333,333 shares of our common stock. 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, pursuant to which we have issued and sold approximately $100.0 million of securities in January 2024 and under 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. For example, from January 1, 2024 through December 31, 2024, the sales price of our common stock ranged from a high of $10.84 to a low of $5.19 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:

- 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;
- our success in commercializing any product candidates for which we obtain marketing approval;
- 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, including interest rates and inflation; 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 no longer qualify as a "smaller reporting company" and, commencing with our Quarterly Report on Form 10-Q for the quarter ending March 31, 2025, we may no longer take advantage of reduced disclosure and reporting requirements applicable to smaller reporting companies, which will require us to incur significant expenses and expend time and resources.

We no longer qualify as a "smaller reporting company" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, based on our non-affiliate public float in excess of $250 million and our annual revenues in excess of $100 million during our last fiscal year, in each case determined as of the last business day of our second quarter of 2024. As a smaller reporting company, we were permitted and relied on exemptions from certain disclosure

requirements that are applicable to other public companies that are not smaller reporting companies. These exemptions included:

- 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 continue to take advantage of some or all of the available exemptions through the filing of this Annual Report on Form 10-K for the year ended December 31, 2024, and any portions of our definitive proxy statement relating to our 2025 Annual Meeting of Stockholders incorporated by reference herein. 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.

Following the filing of this Annual Report and the definitive proxy statement relating to our 2025 Annual Meeting of Stockholders, we will be required to comply with disclosure requirements that are applicable to other public companies that are not smaller reporting companies. Compliance with these additional requirements may increase our legal and financial compliance costs and divert the attention of management and other personnel from operational and other business matters to these additional public company reporting requirements. If we are not able to comply with changing requirements in a timely manner, the market price of our stock could decline, and we could be subject to delisting proceedings by the Nasdaq Global Select Market or sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

We have 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. In January 2021, a putative class action lawsuit was filed against us and certain of our current and former officers and directors. In July 2021, the lead plaintiff voluntarily dismissed the action without prejudice against all defendants and as to all claims, and this action is no longer pending. Nonetheless, due to the volatility in, or the unfulfilled expectations of stockholders for, our stock price, we may be the target of similar litigation in the future.

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

We 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.

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, 2024, we had both federal and state net operating loss, or NOL, carryforwards of $20.0 million and $0.8 million, respectively. The state NOLs will expire beginning in 2041 while the federal NOLs do not expire. These state NOL carryforwards could expire unused and be unavailable to offset our future income tax liabilities. 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 Families First Coronavirus Response 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 Internal Revenue Code, or 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

None.

ITEM 1C. CYBERSECURITY

Cybersecurity Risk Management and Oversight

We have processes for assessing, identifying, and managing cybersecurity risks, integrated into our overall risk management program and information technology function. These processes are designed to:

- Protect our information assets and operations from internal and external cyber threats,
- Safeguard employee, vendor, and collaborator information from unauthorized access or attack, and
- Secure our networks and systems.

Our cybersecurity framework includes physical, procedural, and technical safeguards, as well as:

- Continuous security monitoring to detect any anomalies and events,
- Response plans for cyber incidents,
- Regular system testing and incident simulations, and
- Routine reviews of policies and procedures to identify risks and enhance practices.

To strengthen our cybersecurity risk management practices and oversight, we engage external consultants with expertise in information security, incident response, and governance. Additionally, we evaluate the internal risk oversight programs of third-party service providers before engaging them in order to help protect us from any related vulnerabilities.

Board and Audit Committee Oversight

We do not believe that there are currently any known risks from cybersecurity threats that are reasonably likely to materially impact the company or its business strategy, operations, or financial condition. The Audit Committee provides direct oversight of cybersecurity risk and updates the Board of Directors on such matters.

Management delivers quarterly cybersecurity updates to the Audit Committee, with additional updates provided as significant new threats or incidents arise.

Operational Leadership and Incident Response

Our Vice President of Information Technology, or VP of IT, leads company-wide cybersecurity strategy, policy, standards, and processes. This role includes working across departments to assess and address cybersecurity risks and participating in management's updates to the Audit Committee.

In the event of a cybersecurity incident, the VP of IT collaborates with the information technology department and relevant teams to assess and respond to the incident, determining the need for internal and external reporting.

Our VP of IT brings over 15 years of experience in cybersecurity, including serving as Chief Information Security Officer for a multinational company in the specialty materials industry. Our VP of IT has experience with compliance programs for cybersecurity-related regulations and standards.

Additionally, the VP of IT has participated in Gartner cybersecurity programs and conferences and received training on combating cyber threats, including phishing, malware, and social engineering.

Employee Training and Technology-Based Safeguards

We provide annual data protection and cybersecurity training for all personnel, including full-time, part-time, and temporary staff. This program covers topics such as:

- Social engineering and phishing awareness,
- Password protection and mobile security, and
- Incident response and reporting.

To complement employee training, we utilize technology-based tools and practices to mitigate cybersecurity risks, including:

- Proactive cybersecurity monitoring for threat detection and swift response,
- Tools to address vulnerabilities and protect information assets,
- Endpoint security measures, geo-fencing, and geo-blocking on firewalls, and
- Automatic email prioritization to help our information technology department efficiently address the most critical threats.

ITEM 2. PROPERTIES

Our corporate headquarters 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 93,449 square feet located in Lexington, Massachusetts. Our lease in Cambridge expires in 2026 and our lease in Lexington expires in 2031. We have subleased our office and laboratory space in Cambridge to a third party.

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, 2024, 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 3, 2025, there were approximately 10 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.

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 whose mission is to leverage the power of human genetics to modify the course of and ultimately cure neurological diseases. Our pipeline includes programs for Alzheimer's disease, or AD; Friedreich's ataxia, or FA; Parkinson's disease; and multiple other diseases of the central nervous system, or CNS. Many of our programs are derived from our TRACER™ (Tropism Redirection of AAV by Cell-type-specific Expression of RNA) adeno-associated virus, or AAV, capsid discovery platform, which we have used to generate novel capsids, or TRACER Capsids, and identify associated receptors to potentially enable high brain penetration with genetic medicines following intravenous, or IV, dosing. Some of our programs are wholly-owned, and some are advancing with licensees and collaborators including Alexion, AstraZeneca Rare Disease, or Alexion; Novartis Pharma AG, or Novartis; and Neurocrine Biosciences, Inc., or Neurocrine.

We are advancing our own proprietary pipeline of drug candidates for neurological diseases, with a focus on AD, and particularly on tau, which we view as a critically important AD target. Our wholly-owned prioritized pipeline includes two tau targeting programs: VY7523 (which we formerly referred to as VY-TAU01), an anti-tau antibody for AD and VY1706, a tau silencing gene therapy for AD. The murine version of VY7523 reduced tau spread by more than 60% in preclinical studies. VY7523 demonstrated an acceptable safety, tolerability, and immunogenicity profile as well as expected pharmacokinetic results in a Phase 1, single ascending dose, or SAD, clinical trial in healthy volunteers. In February 2025, we initiated a Phase 1 multiple ascending dose, or MAD, clinical trial of VY7523 in early AD patients. We believe this trial has the potential to generate proof-of-concept data for slowing the spread of pathological tau via tau positron emission tomography imaging in the second half of 2026. VY1706 was selected as the development candidate for the tau silencing gene therapy in November 2024. In a non-human primate, or NHP, study, a single 1.3E13 vector genomes per kilogram dose of VY1706 delivered intravenously resulted in reductions in tau mRNA levels of 50% to 73% across the cerebral cortex, including in areas of the brain where tau accumulates during progression of AD. We anticipate submission of an investigational new drug, or IND, for the VY1706 program in 2026. Our proprietary pipeline also includes early research initiatives to develop a vectorized anti-amyloid antibody for AD and a vectorized superoxide dismutase 1, or SOD1, knockdown gene therapy for SOD1 amyotrophic lateral sclerosis.

We are also working with our collaboration partners on multiple programs. We are advancing seven gene therapy programs with Neurocrine. Development candidates were selected for three of these programs in 2024, resulting in milestone payments to us. We expect that Neurocrine will submit IND filings in 2025 for the two most advanced of these programs, a glucosylceramidase beta 1, or GBA1, gene therapy program for Parkinson's disease and other GBA1-mediated diseases, or the GBA1 Program, and a frataxin, or FXN, gene therapy program for FA, or the FA Program. These two programs are particularly significant to us for two reasons: the subsequent clinical trials of these programs have the potential to establish human proof-of-concept for the TRACER Capsids, and we have the option to opt-in on co-development and co-commercialization in the United States. for both products. In addition to the Neurocrine collaborations, we have partnered with Novartis on TRACER Capsid-based gene therapies for spinal muscular atrophy

and Huntington's disease. We have also licensed capsids to Novartis for three undisclosed CNS targets and to Alexion for one undisclosed rare neurological disease target. In total, these partnerships have delivered more than $500.0 million in non-dilutive funding to us to date, including upfront fees, development milestone payments, option exercise fees, license fees, and research and development expense reimbursement. Looking forward, we have the potential to earn up to $8.2 billion in milestone payments across the partnered portfolio, including $2.9 billion in potential development milestone payments, as well as royalties.

All of the gene therapies in our wholly-owned and collaborative pipeline leverage TRACER. TRACER is a broadly applicable, RNA-based screening platform that enables rapid discovery of AAV capsids with robust penetration of the blood-brain barrier, or BBB, and enhanced CNS tropism in multiple species, including NHPs. We are also developing a second non-viral therapeutics platform focused on non-viral receptor-mediated transport across the BBB.

Despite reporting $132.3 million in net income for the year ended December 31, 2023, we have a history of incurring significant losses. We reported a net loss of $65.0 million for the year ended December 31, 2024, and we reported a net loss of $46.4 million for the year ended December 31, 2022. As of December 31, 2024, we had an accumulated deficit of $326.2 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially in the long term in connection with our ongoing activities, as we:

- conduct clinical trials in connection with our anti-tau antibody program;
- continue investing in our proprietary antibody program, non-viral therapeutics platform, gene therapy and vectorized antibody platforms and programs, and other research and development initiatives;
- continue investing in and supporting TRACER, our proprietary discovery platform to facilitate the selection of AAV capsids and our investment to discover TRACER Capsids with broad tropism in CNS and other tissues with cell-specific transduction properties for particular therapeutic applications;
- increase our investment in the discovery and development of modalities for receptor-mediated non-viral delivery of therapeutic payloads to the CNS;
- 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 our collaboration and license agreement with Neurocrine entered into in January 2019, or the 2019 Neurocrine Collaboration Agreement, our GBA1 Program, pursuant to our collaboration and license agreement with Neurocrine entered into in January 2023, or the 2023 Neurocrine Collaboration Agreement, and our Huntington's disease program, or the Novartis HD Program, pursuant to our license and collaboration agreement with Novartis entered into in December 2023, or the 2023 Novartis 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 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;
- increase our clinical trial insurance coverage as we expand our clinical trials and increase our product liability insurance once we engage in commercialization efforts; and
- continue to operate as a public company.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the foreseeable future. For the year ended December 31, 2024, we recognized $49.7 million of collaboration revenue from the 2023 Neurocrine Collaboration Agreement, $15.0 million of collaboration revenue from an amendment, or the Novartis Amendment, to our option and license agreement with Novartis entered into in March 2022, or the 2022 Novartis Option and License Agreement, $10.4 million of collaboration revenue from the 2019 Neurocrine Collaboration Agreement, and $4.9 million of collaboration revenue from the 2023 Novartis Collaboration Agreement. For additional information about our revenue recognition policy, see the section titled "Summary of significant accounting policies and basis of presentation."

For the foreseeable future, we expect substantially all of our revenue will be generated from the 2019 Neurocrine Collaboration Agreement, the 2023 Neurocrine Collaboration Agreement, the 2023 Novartis Collaboration Agreement, the 2022 Novartis Option and License Agreement, and our option and license agreement with Alexion entered into on October 1, 2021, or the Alexion 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 proprietary antibody, gene therapy, vectorized antibody, and non-viral therapeutic platforms and programs 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 and clinical 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 and clinical 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. During the year ended December 31, 2024, our research and development expenses have increased as compared to the amounts recorded in the same period in the prior year. As our research and development programs progress and as we identify product candidates and initiate preclinical studies and clinical trials, including our clinical trials to evaluate VY7523, we expect research and development costs to continue to increase. 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 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 participants 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, information technology, 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.

During the year ended December 31, 2024, our general and administrative expenses have remained consistent with the amount recorded in the same period in prior year.

Other Income, Net

Other income, net consists primarily of 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 that certain aspects of our accounting policy on revenue recognition require the most significant judgments and estimates in the preparation of our financial statements.

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 and/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. Given the nature of the milestone payments in our contracts with customers, most of the variable consideration is subject to a constraint that does not involve significant judgement.

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. We do not believe that reasonable changes in the assumptions used to determine stand-alone selling price for our performance obligations would materially impact the amount of revenue we recognize.

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.

A significant portion of revenue recognized from the 2019 Neurocrine Collaboration Agreement and the 2023 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 use judgement in estimating the expected remaining costs to complete the research and development services for each performance obligation based on discussions with the Joint Steering Committee for the program and discussions with our collaboration partners. 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 can result in significant changes to the amount of revenue we recognize each period.

Results of Operations

Comparison of the years ended December 31, 2024 and 2023:

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023, respectively, together with the changes in those items in dollars:

	Year ended December 31,		
	2024	2023	Change
		(in thousands)	
Collaboration revenue	$ 80,001	$ 250,008	$ (170,007)
Operating expenses:			
Research and development	127,368	92,172	35,196
General and administrative	35,920	35,822	98
Total operating expenses	163,288	127,994	35,294
Other income, net:			
Interest income	18,328	11,721	6,607
Other income	622	3	619
Total other income, net	18,950	11,724	7,226
(Loss) income before income taxes	(64,337)	133,738	(198,075)
Income tax provision	665	1,408	(743)
Net (loss) income	$ (65,002)	$ 132,330	$ (197,332)

Collaboration Revenue

Collaboration revenue was $80.0 million and $250.0 million for the years ended December 31, 2024 and 2023, respectively. During the year ended December 31, 2024, we recognized collaboration revenue in connection with the following agreements:

- $49.7 million under the 2023 Neurocrine Collaboration Agreement;
- $15.0 million of collaboration revenue from the Novartis Amendment;
- $10.4 million under the 2019 Neurocrine Collaboration Agreement; and
- $4.9 million under the 2023 Novartis Collaboration Agreement.

During the year ended December 31, 2023, we recognized collaboration revenue in connection with the following agreements:

- $79.0 million upon Novartis' decision to exercise two of its license options under the 2022 Novartis Option and License Agreement, or Novartis License Options, along with the expiration of a third Novartis License Option, all of which were determined to be material rights in the 2022 Novartis Option and License Agreement;
- $80.8 million under the 2023 Neurocrine Collaboration Agreement;
- $80.0 million under the 2023 Novartis Collaboration Agreement;
- $9.8 million under the 2019 Neurocrine Collaboration Agreement; and
- $0.4 million under other agreements.

Research and Development Expense

Research and development expense increased by $35.2 million from $92.2 million for the year ended December 31, 2023, to $127.4 million for the year ended December 31, 2024. The following table summarizes our research and development expenses for the years ended December 31, 2024 and 2023. All amounts for the year ended December 31, 2023, have been reclassified to conform to the current year's presentation.

	Year ended December 31,		
	2024	2023	Change
		(in thousands)	
Internal research and development	$ 38,422	$ 27,860	$ 10,562
External research and development	58,081	46,008	12,073
Facilities and other	30,865	18,304	12,561
Total research and development expenses	$ 127,368	$ 92,172	$ 35,196

The increase in research and development expense for the year ended December 31, 2024 was primarily attributable to the following:

- approximately $12.6 million for facility and other costs primarily related to our lease for additional laboratory and office space at 75 Hayden Avenue in Lexington, Massachusetts, which we took occupancy of on February 1, 2024, along with an impairment charge on our leased office and laboratory space in Cambridge, Massachusetts;

- approximately $12.1 million for external research and development costs related to increased program-related spending; and

- approximately $10.6 million for increased internal research and development costs associated with higher headcount in research and development functions as compared to the same period in the prior year.

General and Administrative Expense

General and administrative expense balance remained consistent for the year ended December 31, 2024, compared to December 31, 2023.

Other Income, Net

Other income, net of approximately $19.0 million was recognized during the year ended December 31, 2024, as compared to $11.7 million during the year ended December 31, 2023. Other income, net during the year ended December 31, 2024, was primarily related to interest income due to increased interest rates on increased balances of marketable securities, as our marketable securities increased during the year ended December 31, 2024, as compared to the year ended December 31, 2023.

Liquidity and Capital Resources

Sources of Liquidity

We have funded our operations primarily through private placements of redeemable convertible preferred stock, public offerings and private placements of our common stock, strategic collaborations and option and license arrangements, including our 2019 Neurocrine Agreement, 2023 Neurocrine Collaboration Agreement, 2022 Novartis Agreement, 2023 Novartis Collaboration Agreement, Alexion Agreement, and with our prior collaboration agreements.

As of December 31, 2024, we had cash, cash equivalents, and marketable securities of $332.4 million. Based upon our current operating plan, we expect that our existing cash, cash equivalents, and marketable securities at December 31, 2024, along with amounts expected to be received as reimbursement for development costs under our collaboration and license agreements with Neurocrine and Novartis and interest income, to be sufficient to meet our planned operating expenses and capital expenditure requirements into mid-2027.

Cash Flows

The following table provides information regarding our cash flows:

	Year ended December 31,		
	2024	2023	2022
		(in thousands)	
Net cash (used in) provided by:			
Operating activities	$ (15,310)	$ 77,919	$ (12,509)
Investing activities	(94,859)	(141,643)	(7,339)
Financing activities	114,015	33,645	1,110
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ 3,846	$ (30,079)	$ (18,738)

Cash Flows from Operating Activities

Net cash used in operating activities was $15.3 million during the year ended December 31, 2024. The cash used in operating activities for the year ended December 31, 2024, was primarily driven by our net loss for the year ended December 31, 2024, of $65.0 million and a decrease in deferred revenue of $44.8 million due to revenue recognized under the 2019 Neurocrine Agreement and the 2023 Neurocrine Collaboration Agreement, offset by a decrease in accounts receivable of $78.6 million due to the collection of the upfront payment under the 2023 Novartis Agreement, and stock-based compensation expense of $14.8 million.

Net cash provided by operating activities was $77.9 million during the year ended December 31, 2023. The cash provided by operating activities for the year ended December 31, 2023, was primarily driven by our net income for the year ended December 31, 2023, of $132.3 million, stock-based compensation expense of $11.2 million, and an increase in deferred revenue of $9.4 million, offset by an increase in accounts receivable of $80.2 million due to the recording of the upfront payment under the 2023 Novartis Agreement.

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 in connection with our entry into the 2022 Novartis Option and License Agreement during the year ended December 31, 2022.

Cash Flows from Investing Activities

Net cash used in investing activities was $94.9 million during the year ended December 31, 2024. The cash used in investing activities for the year ended December 31, 2024 was primarily due to $465.7 million for purchases of marketable securities and $3.5 million for purchases of property and equipment, offset by $374.3 million from proceeds from maturities and sales of marketable securities.

Net cash used in investing activities was $141.6 million during the year ended December 31, 2023. The cash used in investing activities for the year ended December 31, 2023 was primarily due to $224.0 million for purchases of marketable securities and $3.3 million for purchases of property and equipment, offset by $85.6 million from proceeds from maturities and sales of marketable securities.

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.

Cash Flows from Financing Activities

Net cash provided by financing activities was $114.0 million during the year ended December 31, 2024 primarily due to the $93.5 million in net proceeds from a public offering of common stock and warrants and $19.3 million in connection with the sale of common stock to Novartis in January 2024.

Net cash provided by financing activities was $33.6 million during the year ended December 31, 2023 primarily due to the $31.1 million in proceeds from the sale of common stock in connection with the 2023 Neurocrine Collaboration Agreement along with 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 $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.

Funding Requirements

Our expenses increased during the year ended December 31, 2024 as compared with the prior year as our development programs progressed and we increased headcount. We expect our expenses to continue to increase as we continue the research and development of, conduct clinical trials of, and seek marketing approval for our product candidates including our Phase 1 MAD clinical trial to evaluate VY7523 in 2025, 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 employees 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.

As of December 31, 2024, we had cash, cash equivalents, and marketable securities of $332.4 million. Based upon our current operating plan, we expect that our existing cash, cash equivalents, and marketable securities at December 31, 2024, along with amounts expected to be received as reimbursement for development costs under our collaboration and license agreements with Neurocrine and Novartis and interest income, to be sufficient to meet our

planned operating expenses and capital expenditure requirements into mid-2027. 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, including our clinical trials to evaluate VY7523;
- 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 arrangements we may enter into in the future, including any research and development costs for which we are responsible, future additional obligations that we may be committed to in connection with these agreements, and our receipt of any expense reimbursements, 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 license agreement we entered into with Touchlight IP Limited in November 2022;
- 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 licensees 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 products or 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, 2024, we ceased to qualify as a smaller reporting company, which requires 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, 2024, and any portions of our definitive proxy statement relating to our 2025 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 a material effect on our business, financial condition, or results of operations during the year ended December 31, 2024.

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 of 1934, or 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 Securities and Exchange Commission'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, 2024. 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, 2024, 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, 2024 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, 2024.

Our independent registered public accounting firm, Ernst & Young LLP, issued an attestation report on our internal control over financial reporting, which is included herein.

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, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

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

Opinion on Internal Control Over Financial Reporting

We have audited Voyager Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Voyager Therapeutics, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2024 and 2023, 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, 2024, and the related notes and our report dated March 11, 2025 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's 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. Also, 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.

/s/ Ernst & Young LLP Boston, Massachusetts March 11, 2025

ITEM 9B. OTHER INFORMATION

(c) Director and Officer Trading Arrangements

A portion of the compensation of our directors and officers (as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) is in the form of equity awards and, from time to time, directors and officers engage in open-market transactions with respect to the securities acquired pursuant to such equity awards or our other securities, including to satisfy tax withholding obligations when equity awards vest or are exercised, for diversification or other personal reasons.

Transactions in our securities by directors and officers are required to be made in accordance with our insider trading policy, which requires that the transactions be in accordance with applicable U.S. federal securities laws that prohibit trading while in possession of material nonpublic information. Rule 10b5-1 under the Exchange Act provides an affirmative defense that enables directors and officers to prearrange transactions in our securities in a manner that avoids concerns about initiating transactions while in possession of material nonpublic information.

The following table describes, for the fourth quarter of fiscal year 2024, each trading arrangement for the sale or purchase of our securities adopted or terminated by our directors and officers that is either (1) a contract, instruction or written plan intended to satisfy the affirmative defense conditions of Rule 10b5-1(c), or a Rule 10b5-1 trading arrangement, or (2) a non-Rule 10b5-1 trading arrangement, as defined in Item 408(c) of Regulation S-K.

Name (Title)	Action Taken (Date of Action)	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Trading Arrangement	Aggregate Number of Securities
Nathan Jorgensen, Ph.D. (Chief Financial Officer)	Adoption (November 21, 2024)	Durable Non-Rule 10b5-1 trading arrangement for sell-to-cover transactions related to restricted stock units (“RSUs”) granted on or after July 8, 2024	Sale	Until final settlement of any covered RSU	Indeterminable[(1)]
Jacquelyn Fahey Sandell (Chief Legal Officer)	Adoption (December 2, 2024)	Rule 10b5-1 trading arrangement for exercises of options and sale of shares	Sale	Until January 30, 2026, or such earlier date upon which all transactions are completed or expire without execution	Up to 46,987 shares
Robin Swartz (Chief Operating Officer and Chief Business Officer)	Adoption (December 5, 2024)	Rule 10b5-1 trading arrangement for exercises of options and sale of shares	Sale	Until May 29, 2026, or such earlier date upon which all transactions are completed or expire without execution	Up to 70,985 shares

(1) The number of shares subject to covered RSUs that will be sold to satisfy applicable tax withholding obligations upon vesting is unknown as the number will vary based on the extent to which vesting conditions are satisfied, the market price of the company’s common stock at the time of settlement, and the potential future grant of additional RSUs subject to this arrangement. This trading arrangement, which applies to RSUs whether vesting is based on the passage of time and/or the achievement of performance goals, provides for the automatic sale of shares that would otherwise be issuable on each settlement date of a covered RSU in an amount sufficient to satisfy the applicable withholding obligation, with the proceeds of the sale delivered to the company in satisfaction of the applicable withholding obligation.

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 2025 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 2025 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 2025 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 2025 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 2025 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.

	Pages
Report of independent registered public accounting firm PCAOB ID 42	F-1
Consolidated Balance Sheets	F-3
Consolidated Statements of Operations and Comprehensive (Loss) Income	F-4
Consolidated Statements of Stockholders' Equity	F-5
Consolidated Statements of Cash Flows	F-6
Notes to consolidated financial statements	F-7

(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.

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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, 2024 and 2023, 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, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated March 11, 2025 expressed an unqualified opinion thereon.

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 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. 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 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 a 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 of the consolidated financial statements, the Company recorded collaboration revenue of $46.4 million for the year ended December 31, 2024 under the proportional performance method, and had total deferred revenue of $30.4 million. The Company recognizes arrangement consideration allocated to certain performance obligations that are delivered over time 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

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's revenue recognition under the proportional performance method, including controls over the evaluation of the completeness and accuracy of the underlying data used to determine the actual costs incurred and the expected remaining costs to complete the research and development services for each performance obligation that is accounted for using the proportional performance method.

Our audit procedures included, among others, 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 that is accounted for using the proportional performance method. We performed inquiries of research and development personnel and reviewed the minutes of Joint Steering Committee meetings to validate management's estimates and 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 11, 2025

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

	December 31,	
	2024	**2023**
Assets		
Current assets:		
Cash and cash equivalents	$ 71,367	$ 68,802
Marketable securities	195,317	162,073
Accounts receivable	1,504	80,150
Related party collaboration receivable	676	3,341
Prepaid expenses and other current assets	7,945	5,318
Total current assets	276,809	319,684
Property and equipment, net	14,314	16,494
Restricted cash	2,874	1,593
Marketable securities, non-current	65,704	—
Operating lease, right-of-use assets	33,349	13,510
Total assets	$ 393,050	$ 351,281
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,996	$ 1,604
Accrued expenses	14,171	16,823
Operating lease liabilities	7,227	3,200
Deferred revenue, current	24,394	42,881
Total current liabilities	49,788	64,508
Operating lease liabilities, net of current portion	36,499	17,094
Deferred revenue, non-current	6,003	32,359
Other non-current liabilities	1,000	1,000
Total liabilities	93,290	114,961
Commitments, contingencies, and other liabilities (see note 8)		
Stockholders' equity:		
Preferred stock, $0.001 par value: 5,000,000 shares authorized; no shares issued and outstanding at December 31, 2024 and 2023	—	—
Common stock, $0.001 par value: 120,000,000 shares authorized; 54,731,316 and 44,038,333 shares issued and outstanding at December 31, 2024 and 2023, respectively	55	44
Additional paid-in capital	626,296	497,506
Accumulated other comprehensive loss	(407)	(48)
Accumulated deficit	(326,184)	(261,182)
Total stockholders' equity	299,760	236,320
Total liabilities and stockholders' equity	$ 393,050	$ 351,281

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,		
	2024	**2023**	**2022**
Collaboration revenue	$ 80,001	$ 250,008	$ 40,907
Operating expenses:			
Research and development	127,368	92,172	60,764
General and administrative	35,920	35,822	30,980
Total operating expenses	163,288	127,994	91,744
Operating (loss) income	(83,287)	122,014	(50,837)
Other income, net:			
Interest income	18,328	11,721	1,792
Other income	622	3	2,653
Total other income, net	18,950	11,724	4,445
(Loss) income before income taxes	(64,337)	133,738	(46,392)
Income tax provision	665	1,408	16
Net (loss) income	$ (65,002)	$ 132,330	$ (46,408)
Other comprehensive (loss) income			
Net unrealized (loss) gain on available-for-sale-securities	(359)	171	(81)
Total other comprehensive (loss) income	(359)	171	(81)
Comprehensive (loss) income	$ (65,361)	$ 132,501	$ (46,489)
Net (loss) income per share, basic	$ (1.13)	$ 3.08	$ (1.21)
Net (loss) income per share, diluted	$ (1.13)	$ 2.97	$ (1.21)
Weighted-average common shares outstanding, basic	57,667,543	43,020,747	38,356,810
Weighted-average common shares outstanding, diluted	57,667,543	44,569,334	38,356,810

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) Income	Deficit	Equity
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
Exercises of vested stock options	385,655	1	1,851	—	—	1,852
Vesting of restricted stock units	531,560	—	—	—	—	—
Issuance of common stock in connection with the 2023 Neurocrine Collaboration Agreement	4,395,588	5	31,116	—	—	31,121
Issuance of common stock under ESPP	111,639	—	959	—	—	959
Stock-based compensation expense	—	—	10,867	—	—	10,867
Unrealized gain on available-for-sale securities	—	—	—	171	—	171
Net income	—	—	—	—	132,330	132,330
Balance at December 31, 2023	44,038,333	$ 44	$ 497,506	$ (48)	$ (261,182)	$ 236,320
Exercises of vested stock options	106,831	—	388	—	—	388
Vesting of restricted stock units	515,303	1	—	—	—	1
Issuance of common stock in connection with the 2023 Novartis Stock Purchase Agreement	2,145,002	2	19,303	—	—	19,305
Issuance of common stock and pre-funded warrants in connection with underwritten public offering	7,777,778	8	93,465	—	—	93,473
Issuance of common stock under ESPP	148,069	—	1,172	—	—	1,172
Stock-based compensation expense	—	—	14,462	—	—	14,462
Unrealized loss on available-for-sale securities	—	—	—	(359)	—	(359)
Net loss	—	—	—	—	(65,002)	(65,002)
Balance at December 31, 2024	54,731,316	$ 55	$ 626,296	$ (407)	$ (326,184)	$ 299,760

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,		
	2024	**2023**	**2022**
Cash flow from operating activities			
Net (loss) income	$ (65,002)	$ 132,330	$ (46,408)
Adjustments to reconcile net (loss) income to net cash (used in) provided by operating activities:			
Stock-based compensation expense	14,785	11,153	9,344
Depreciation	4,731	4,441	6,191
Amortization of premiums and discounts on marketable securities	(7,969)	(3,626)	(16)
Impairment charge on leased facility	2,776	—	—
Gain on lease termination	—	—	(2,468)
Loss on disposal of fixed assets	510	178	377
Changes in operating assets and liabilities:			
Accounts receivable	78,646	(80,150)	—
Related party collaboration receivable	2,665	(3,084)	475
Prepaid expenses and other assets	(2,627)	76	(1,967)
Operating lease, right-of-use assets	4,597	1,975	3,462
Other non-current assets	—	—	(152)
Accounts payable	2,392	(962)	1,992
Accrued expenses	(2,652)	9,007	(3,148)
Operating lease liabilities	(3,320)	(2,833)	(3,922)
Deferred revenue	(44,842)	9,414	23,731
Net cash (used in) provided by operating activities	(15,310)	77,919	(12,509)
Cash flow from investing activities			
Purchases of property and equipment	(3,521)	(3,256)	(2,491)
Purchases of marketable securities	(465,685)	(223,968)	(54,848)
Proceeds from sales and maturities of marketable securities	374,347	85,581	50,000
Net cash used in investing activities	(94,859)	(141,643)	(7,339)
Cash flow from financing activities			
Proceeds from the exercise of stock options	388	1,852	629
Proceeds from the issuance of common stock in connection with the underwritten public offering	93,473	—	—
Proceeds from the issuance of common stock in connection with the 2023 Novartis Stock Purchase Agreement	19,305	—	—
Proceeds from the issuance of common stock in connection with the 2023 Neurocrine Collaboration Agreement	—	31,121	—
Proceeds from the purchase of common stock under ESPP	849	672	481
Net cash provided by financing activities	114,015	33,645	1,110
Net increase (decrease) in cash, cash equivalents, and restricted cash	3,846	(30,079)	(18,738)
Cash, cash equivalents, and restricted cash beginning of period	70,395	100,474	119,212
Cash, cash equivalents, and restricted cash end of period	$ 74,241	$ 70,395	$ 100,474
Supplemental disclosure of cash and non-cash activities			
Operating lease right-of-use asset obtained in exchange for operating lease liability	$ 26,751	$ —	$ —
Capital expenditures incurred but not yet paid	$ —	$ —	$ 14

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 whose mission is to leverage the power of human genetics to modify the course of and ultimately cure neurological diseases. Its pipeline includes programs for Alzheimer's disease ("AD"); Friedreich's ataxia ("FA"); Parkinson's disease; and multiple other diseases of the central nervous system ("CNS"). Its pipeline also includes other programs it wholly owns and programs which it is advancing with licensees and collaborators including Alexion, AstraZeneca Rare Disease, or Alexion; Novartis Pharma AG, or Novartis; and Neurocrine Biosciences, Inc., or Neurocrine, for the treatment of multiple other diseases of the central nervous system, or CNS.

Many of its programs are derived from the Company's TRACER™ (Tropism Redirection of AAV by Cell-type-specific Expression of RNA) adeno-associated virus ("AAV") capsid discovery platform, which it has used to generate novel capsids ("TRACER Capsids") and identify associated receptors to potentially enable high brain penetration with genetic medicines following intravenous ("IV") dosing. TRACER is a broadly applicable, RNA-based screening platform that enables rapid discovery of AAV capsids with robust penetration of the blood-brain barrier ("BBB") and enhanced CNS tropism in multiple species, including non-human primates. The Company is also developing a second non-viral therapeutics platform focused on non-viral receptor-mediated transport across the BBB.

Despite reporting net income for the year ended December 31, 2023, the Company has a history of incurring significant losses. As of December 31, 2024, the Company had an accumulated deficit of $326.2 million. The Company has not generated any product revenue and has financed its operations primarily through public offerings and private placements of its equity securities and funding from fees, milestone payments, and cost reimbursements associated with its prior and current collaborations and license agreements.

As of December 31, 2024, the Company had cash, cash equivalents, and marketable securities of $332.4 million. Based upon its current operating plan, the Company expects that its existing cash, cash equivalents, and marketable securities at December 31, 2024 to be sufficient to meet the Company's planned operating expenses and capital expenditure requirements for at least twelve months from the issuance of these consolidated financial statements.

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, research and development 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 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 or credit losses have been recognized.

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

Cash equivalents and marketable securities as of December 31, 2024, and 2023 consist of the following:

	Amortized Cost	Unrealized Gains	Unrealized Losses		Fair Value
			Less than 12 months	Greater than 12 months	
	(in thousands)				
As of December 31, 2024					
Money market funds included in cash and cash equivalents	$ 59,658	$ —	$ —	$ —	$ 59,658
Marketable securities:					
U.S. Treasury notes	125,996	32	(45)	(200)	125,783
U.S. Government agency securities	27,552	6	(5)	(35)	27,518
Certificates of deposit	4,280	6	—	—	4,286
Corporate bonds	95,016	18	(58)	—	94,976
Commercial paper	8,456	2	—	—	8,458
Total money market funds and marketable securities	$ 320,958	$ 64	$ (108)	$ (235)	$ 320,679
As of December 31, 2023					
Money market funds included in cash and cash equivalents	$ 65,589	$ —	$ —	$ —	$ 65,589
Marketable securities:					
U.S. Treasury notes	102,966	81	(3)	—	103,044
U.S. Government agency securities	31,068	10	(3)	—	31,075
Corporate bonds	23,975	2	(7)	—	23,970
Commercial paper	3,985	—	—	—	3,985
Total money market funds and marketable securities	$ 227,583	$ 93	$ (13)	$ —	$ 227,663

All of the Company's marketable securities at December 31, 2024, and 2023 have a contractual maturity of two years or less.

As of December 31, 2024, the Company held 97 marketable securities that were in an unrealized loss position, representing $156.3 million in fair value. As of December 31, 2023, the Company held 14 marketable securities that were in an unrealized loss position, representing $44.2 million in fair value. The unrealized losses at December 31, 2024, and December 31, 2023, were attributable to changes in interest rates and the unrealized losses do not represent credit losses. The Company does not intend to sell these securities, and it is likely that it will not be required to sell them before recovery of their amortized cost basis.

Restricted Cash

As of December 31, 2024, and 2023, the Company maintained restricted cash totaling approximately $2.9 million and $1.6 million, respectively, held in the form of money market accounts as collateral for the Company's facility lease obligations. 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,	
	2024	2023
	(in thousands)	
Cash and cash equivalents	$ 71,367	$ 68,802
Restricted cash	2,874	1,593
Total cash, cash equivalents, and restricted cash	$ 74,241	$ 70,395

Property and Equipment, net

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 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 through December 31, 2024, other than with respect to the right-of-use asset for one of the Company's leases.

In June 2024, the Company vacated its leased office and laboratory space in Cambridge, Massachusetts. The Company recorded an impairment charge of $2.8 million to operating expenses as a result of the carrying value of the leased office and laboratory space asset group exceeding the undiscounted cash flows projected from a planned sublease of the facility. The impairment charge reduced the carrying value of the leased office and laboratory space asset group by $2.8 million.

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.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, in which 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 portion of revenue recognized from the 2019 Neurocrine Collaboration Agreement and the 2023 Neurocrine Collaboration Agreement relate 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, adjusts 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 sheets 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 and comprehensive (loss) income 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 the Company's historical volatility over 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 derived 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, 2024, 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, 2024 and 2022, 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, 2024 and 2022.

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,		
	2024	2023	2022
Unvested restricted common stock awards	—	22,500	45,000
Unvested restricted common stock units	1,649,943	1,370,897	1,112,563
Outstanding stock options	8,800,464	7,425,444	6,199,571
Total	10,450,407	8,818,841	7,357,134

Basic net (loss) income and diluted weighted-average shares outstanding are as follows for the years ended December 31, 2024, 2023, and 2022:

	Year Ended December 31,		
	2024	2023	2022
	(in thousands, except share data)		
Numerator:			
Net (loss) income	$ (65,002)	$ 132,330	$ (46,408)
Denominator for basic net (loss) income per share:			
Weighted average shares outstanding-basic	57,667,543	43,020,747	38,356,810
Denominator for diluted net (loss) income per share:			
Weighted average shares outstanding	57,667,543	43,020,747	38,356,810
Common stock options and restricted stock units	—	1,548,587	—
Weighted average shares outstanding-diluted	57,667,543	44,569,334	38,356,810

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.

Recently Adopted Accounting Pronouncement

In November 2023, the Financial Accounting Standards Board ("FASB") issued ASU No. 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosure*. This standard requires annual and interim disclosure of significant segment expenses that are regularly provided to the CODM. The amendments in this update also expand the interim segment disclosure requirements. The disclosures required under ASU 2023-07 are also required for public entities with a single reportable segment. This standard is effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024. Early adoption is permitted and the amendments in this update are required to be applied on a retrospective basis. The Company has adopted ASU 2023-07 on its consolidated financial statements. and has included the disclosure with this Annual Report on Form 10-K.

Recently Issued Accounting Pronouncement not yet Adopted

In December 2023, the FASB issued ASU 2023-09, "*Income Taxes (Topic 740) - Improvements to Income Tax Disclosures."* ASU 2023-09 enhances the transparency and decision usefulness of income tax disclosures by requiring consistent categories and greater disaggregation of information in the rate reconciliation and income taxes paid disaggregated by jurisdiction. The amendments in ASU 2023-09 are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2024, and is applicable to the Company in fiscal 2025. However, retrospective application is permitted. Early adoption is also permitted. The Company is in the process of evaluating the impact of ASU 2023-09.

3. Fair value measurements

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2024, and 2023 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, 2024				
Money market funds included in cash and cash equivalents	$ 59,658	$ 59,658	$ —	$ —
Marketable securities:				
U.S. Treasury notes	125,783	125,783	—	—
U.S. Government agency securities	27,518	27,518	—	—
Certificates of deposit	4,286	—	4,286	—
Corporate bonds	94,976	—	94,976	—
Commercial paper	8,458	—	8,458	—
Total money market funds and marketable securities	$ 320,679	$ 212,959	$ 107,720	$ —
December 31, 2023				
Money market funds included in cash and cash equivalents	$ 65,589	$ 65,589	$ —	$ —
Marketable securities:				
U.S. Treasury notes	103,044	103,044	—	—
U.S. Government agency securities	31,075	31,075	—	—
Corporate bonds	23,970	—	23,970	—
Commercial paper	3,985	—	3,985	—
Total money market funds and marketable securities	$ 227,663	$ 199,708	$ 27,955	$ —

The Company measures the fair value of money market funds, U.S. Treasury notes and U.S. Government agency securities based on quoted prices in active markets for identical securities. The Company measures the fair value of the Level 2 securities, corporate bonds, certificates of deposit, and commercial paper, based on recent trades of securities in inactive markets or based on quoted market prices of similar instruments and other significant inputs derived from or corroborated by observable market data.

4. Prepaid expenses and other current assets

Prepaid expenses and other current assets consist of the following:

	As of December 31,	
	2024	2023
	(in thousands)	
Other current assets	$ 2,874	$ 2,628
Prepaid insurance	428	607
Prepaid research and development contracts	2,332	1,119
Accrued interest receivable	2,311	964
Total	$ 7,945	$ 5,318

5. Property and equipment, net

Property and equipment, net consists of the following:

	As of December 31,	
	2024	2023
	(in thousands)	
Laboratory equipment	$ 20,339	$ 20,536
Leasehold improvements	6,487	7,106
Furniture and office equipment	2,334	2,625
Other	1,112	1,265
Total property and equipment	30,272	31,532
Less: accumulated depreciation	(15,958)	(15,038)
Property and equipment, net	$ 14,314	$ 16,494

The Company recorded $4.7 million, $4.4 million, and $6.2 million in depreciation expense during the years ended December 31, 2024, 2023, and 2022, respectively.

6. Accrued expenses

Accrued expenses consist of the following:

	As of December 31,	
	2024	2023
	(in thousands)	
Employee compensation costs	$ 6,752	$ 6,614
Research and development costs	5,246	5,225
Accrued goods and services	1,201	4,229
Professional services	972	755
Total	$ 14,171	$ 16,823

7. Lease obligation

Operating Leases

As of December 31, 2024, the Company has a lease for laboratory and office space at 75 Hayden Avenue in Lexington, Massachusetts through January 31, 2031, and a lease for additional office and laboratory space at 64 Sidney Street in Cambridge, Massachusetts (the "Cambridge Facility") through November 30, 2026.

In August 2023, the Company entered into a first amendment (the "First Amendment") to its existing lease for laboratory and office space at 75 Hayden Avenue in Lexington, Massachusetts, pursuant to which the Company agreed to lease approximately 61,307 square feet of additional office and laboratory space. The commencement date for the First Amendment occurred on February 1, 2024. The expected contractual obligation under the First Amendment to the Company's existing lease is approximately $35.4 million, to be paid over the 7 year term of the lease.

The Company's lease agreements require the Company to maintain a cash deposit or irrevocable letter of credit in the aggregate amount of $2.9 million payable to its landlords as security for the performance of its obligations under the leases. These amounts are recorded as restricted cash in the accompanying consolidated balance sheets.

In June 2024, the Company vacated its leased office and laboratory space in Cambridge, Massachusetts. The Company recorded an impairment charge of $2.8 million to operating expenses during the second quarter of 2024 as a result of the carrying value of the leased office and laboratory space asset group exceeding the undiscounted cash flows projected from a planned sublease of the facility. The impairment charge reduced the carrying value of the leased office and laboratory space asset group by $2.8 million. In August 2024, the Company executed the sublease of the Cambridge Facility (the "Sublease Agreement"). Payments received under the Sublease Agreement are included in other income in the condensed consolidated statements of operations and comprehensive (loss) income.

Total lease cost for operating leases of approximately $10.0 million, $3.6 million, and $4.6 million was incurred during the years ended December 31, 2024, 2023, and 2022, respectively. As of December 31, 2024, the weighted average remaining lease term was 4.7 years, and the weighted average incremental borrowing rate used to determine the operating lease liability was 6.8%. As of December 31, 2023, the weighted average remaining lease term was 5.0 years, and the weighted average incremental borrowing rate used to determine the operating lease liability was 7.4%.

The following table summarizes the operating sublease income generated under the Sublease Agreement and the BioNTech Sublease Agreement for the years ended December 31, 2024, 2023, and 2022:

	Years ended December 31,		
	2024	2023	2022
		(in thousands)	
Operating sublease income	$ 601	$ —	$ 1,380

Future minimum lease payments due under operating leases are as follows:

Year Ending December 31,	Total Minimum Lease Payments
	(in thousands)
2025	$ 9,909
2026	9,983
2027	7,763
2028	7,996
2029	8,235
Thereafter	8,710
Total future minimum lease payments	$ 52,595
Less: imputed interest	(8,869)
Total operating lease liabilities	$ 43,726
Reported as:	
Operating lease liabilities	$ 7,227
Operating lease liabilities, net of current portion	36,499
Total operating lease liabilities	$ 43,726

8. Commitments, contingencies, and other liabilities

As of December 31, 2024, and 2023, other current and non-current liabilities consisted of the following:

	As of December 31,	
	2024	2023
	(in thousands)	
Other current liabilities		
Operating lease liabilities	$ 7,227	$ 3,200
Total other current liabilities	$ 7,227	$ 3,200
Other non-current liabilities		
Operating lease liabilities	$ 36,499	$ 17,094
Other	1,000	1,000
Total other non-current liabilities	$ 37,499	$ 18,094

Other Agreements

In 2016, the Company entered into a research and development funding arrangement with a non-profit organization that provided up to $4.0 million in funding to the Company upon the achievement of clinical and development milestones. The agreement as amended in 2022 provides that the Company is obligated to 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. In 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 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, 2024, or 2023.

9. Significant Agreements

2023 Novartis License and Collaboration Agreement

In December 2023 (the "2023 Novartis Collaboration Agreement Effective Date"), the Company entered into a License and Collaboration Agreement (the "2023 Novartis Collaboration Agreement") with Novartis to (a) provide rights to Novartis with respect to certain TRACER Capsids for use in the research, development, and commercialization by Novartis of AAV gene therapy products and product candidates, comprising such TRACER Capsids and payloads intended for the treatment of spinal muscular atrophy (the "Novartis SMA Program") and (b) collaborate to develop AAV gene therapy products and product candidates intended for the treatment of Huntington's disease (the "Novartis HD Program"), in each case, leveraging TRACER Capsids and other intellectual property controlled by the Company.

Novartis SMA Program and Novartis HD Program Licenses

Under the terms of the 2023 Novartis Collaboration Agreement, the Company granted Novartis and its affiliates:

- a non-exclusive, non-transferable, non-sublicensable (except in limited circumstances for contractors), worldwide, royalty-free right and license under any patents or know-how controlled by the Company and related to the TRACER Capsids to evaluate the same for use in the development of a product or product candidate under the Novartis SMA Program (a "Novartis SMA Program Product") comprising such a TRACER Capsid and a payload selected by Novartis during the period beginning on the 2023 Novartis Collaboration

Agreement Effective Date and ending on the third anniversary of the 2023 Novartis Collaboration Agreement Effective Date;

- an exclusive (even as to the Company), sublicensable, non-transferable, worldwide, royalty-bearing right and license under any patents or know-how controlled by the Company and relating to the selected TRACER Capsids to exploit the same as incorporated into a Novartis SMA Program Product for all human and veterinary diagnostic, prophylactic and therapeutic uses during the 2023 Novartis Collaboration Term (as defined below); and

- an exclusive (even as to the Company), non-transferable, sublicensable, worldwide, royalty-bearing right and license under any patents and know-how controlled by the Company and relating to the development of a product or product candidate under the Novartis HD Program (a "Novartis HD Program Product") to exploit the same for all human and veterinary diagnostic, prophylactic and therapeutic uses during the 2023 Novartis Collaboration Term.

Governance

The Company and Novartis have agreed to manage the Novartis HD Program through a Joint Steering Committee until dissolved after the first IND application filing for a Novartis HD Program Product.

Development, Regulatory Approval, Commercialization and Diligence

Under the 2023 Novartis Collaboration Agreement, Novartis is solely responsible for, and has sole decision-making authority with respect to, at its own expense, the exploitation of a Novartis SMA Program Product.

With respect to the Novartis HD Program, the parties have agreed to conduct research and pre-clinical development of Novartis HD Program Products pursuant to a research plan, with Novartis reimbursing the Company for its activities thereunder in accordance with the agreed-to budget. From and after the first IND application filing for the Novartis HD Program, the parties have agreed that Novartis will assume sole responsibility for the development and commercialization of Novartis HD Program Products.

With respect to each of the Novartis SMA Program Products and Novartis HD Program Products, Novartis is obligated to use commercially reasonable efforts to develop and obtain regulatory approval for at least one of each such product in the United States and in certain other international markets specified in the 2023 Novartis Collaboration Agreement.

Termination

Unless earlier terminated, with respect to any licensed product(s) under the 2023 Novartis Collaboration Agreement, on a country-by-country basis, the 2023 Novartis Collaboration Agreement expires upon the expiration of the last-to-expire royalty term with respect to such licensed product in such country in the territory (the "2023 Novartis Collaboration Term"). Novartis may terminate the 2023 Novartis Collaboration Agreement, in whole or in part, for any or no reason upon ninety days' written notice to the Company. The 2023 Novartis Collaboration Agreement may also be terminated by either party under specific circumstances, including the other party's uncured material breach.

Financial Terms

Under the 2023 Novartis Collaboration Agreement, Novartis paid the Company an upfront payment of $80.0 million. The Company is eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of $200.0 million for the Novartis SMA Program and up to an aggregate of $225.0 million for the Novartis HD Program, in each case for the first corresponding product to achieve the corresponding milestone. The Company is also eligible to receive (a) specified sales milestone payments of up to an aggregate of $400.0 million for the Novartis SMA Program and up to an aggregate of $375.0 million for the Novartis HD Program and (b) tiered, escalating royalties in the high single-digit to low double-digit percentages of annual net sales of the Novartis SMA Program Products and the Novartis HD Program Products. The royalties are subject to potential

customary reductions, including patent claim expiration, payments for certain third-party licenses, and biosimilar market penetration, subject to specified limits.

Stock Purchase Agreement

Under the stock purchase agreement with Novartis entered into on December 28, 2023 (the "2023 Novartis Stock Purchase Agreement"), Novartis purchased 2,145,002 shares of common stock of the Company (the "Novartis Shares") for an aggregate purchase price of approximately $20.0 million.

Accounting Analysis

The Company determined the 2023 Novartis Collaboration Agreement represents a contract with a customer under ASC 606. In addition, the 2023 Novartis Collaboration Agreement did not modify the scope or price of the 2022 Novartis Option and License Agreement, as discussed below. The Company therefore determined that the 2023 Novartis Collaboration Agreement should be accounted for separately. The 2023 Novartis Collaboration Agreement includes the following performance obligations: (i) the development and commercialization license for the Novartis SMA Program, (ii) the development and commercialization license for the Novartis HD Program; and (iii) the research and development services for the Novartis HD Program ("Novartis HD Research Services"). The development and commercialization licenses for the Novartis HD Program and Novartis SMA Program are each distinct, as Novartis can benefit from such licenses on their own or from other resources commonly available in the industry given the stage of development of the product candidates subject to the licenses. Similarly, the research and development services for the Novartis HD Program provide a distinct benefit to Novartis within the context of the contract, separate from the licenses.

The transaction consideration allocated to the performance obligations within the 2023 Novartis Collaboration Agreement includes fixed consideration of $80.0 million, and variable consideration, which is comprised of an estimated $24.2 million of cost reimbursements for Novartis HD Research Services, up to $425.0 of potential development milestone payments, up to $775.0 million of potential sales milestone payment, and sales-based royalties. The consideration related to the Novartis HD Research Services, becomes due and payable on a quarterly basis as the services are being performed.

The Company estimates variable consideration using the most likely amount approach. At the outset of the contract, the Company has determined this consideration should be constrained. The sales milestone payments and royalties will be recognized in the period the underlying sales occur, as this consideration is related to the two development and commercialization licenses, the predominant performance obligations in the contract.

The Company allocated the fixed transaction price to the separate performance obligations based on the relative standalone selling price of each performance obligation. The standalone selling prices for development and commercialization licenses for the Novartis SMA Program and Novartis HD Program were estimated using an adjusted-market approach. The Company allocated the variable consideration related to the Novartis HD Research Services as the consideration becomes payable as the Company delivers the Novartis HD Research Services and allocating the entirety of this consideration to the Novartis HD Research Services reflects the amount the Company expects to be entitled to for performing the services. The development milestone payments, the sales milestone payments and the royalties are allocated to the respective development and commercialization licenses for the Novartis SMA Program and Novartis HD Program as the variable consideration relates directly to those performance obligations.

The Company recognized the $80.0 million fixed transaction price allocated to the development and commercialization licenses for the Novartis SMA Program and Novartis HD Program, as collaboration revenue upon delivery of the development and commercialization licenses to Novartis in December 2023 and was collected in January 2024.The issuance of the Novartis Shares to Novartis pursuant to the 2023 Novartis Stock Purchase Agreement in January 2024 resulted in a premium of $0.7 million. The premium was allocated to the development and commercialization licenses for the Novartis HD Program and Novartis SMA Program and was recognized as collaboration revenue during the first quarter of 2024, upon the issuance of the Novartis Shares under the 2023 Novartis Stock Purchase Agreement. The Novartis HD Research Services commenced in the first quarter of 2024. During the year ended December 31, 2024, the Company recognized $4.2 million of collaboration revenue associated with research and

development services performed during the period and the corresponding cost reimbursement receivable for the Novartis HD Program Additionally, as of December 31, 2024, there was $1.5 million of accounts receivable related to reimbursable costs expected to be received from Novartis for research and development services performed.

The Company incurred approximately $1.9 million of business development costs related to the 2023 Novartis Collaboration Agreement which were payable only upon the execution of the agreement and therefore are considered incremental costs of obtaining a contract with a customer. Given the substantial value associated with the development and commercialization licenses for the Novartis SMA Program and Novartis HD Program that were delivered in December 2023, the Company recognized the $1.9 million of costs in general and administrative expenses during the year ended December 31, 2023.

2022 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 "2022 Novartis Agreement"). Pursuant to the 2022 Novartis Agreement, the Company granted Novartis options (the "Novartis License Options") to license TRACER Capsids (the "Novartis Licensed Capsids") for exclusive use in programs targeting three specified genes (the "Initial Novartis Targets"), to develop and commercialize AAV gene therapy candidates comprised of Novartis Licensed Capsids and payloads directed to such targets (the "Novartis Initial Licensed Products"). Effective as of March 1, 2023, Novartis exercised its Novartis License Options to license TRACER Capsids for use in gene therapy programs against two undisclosed programs targeting specified genes (the "Initial Novartis Targets"). Upon Novartis' exercise of the two Novartis License Options for Initial Novartis Targets, the Company granted 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 Novartis Initial Licensed Products. The Company also agreed to provide certain additional know-how to enable Novartis to exploit the Novartis Licensed Capsid and a payload directed to the applicable Initial Novartis Target for use in an Initial Novartis Licensed Product. Novartis elected not to license a capsid for one Initial Novartis Target prior to the expiration of the applicable Novartis License Option. As a result, the non-exclusive research license that the Company granted to Novartis in connection with this third Initial Novartis Target terminated, and all capsid rights with respect to that Initial Novartis Target returned to the Company.

On September 3, 2024, the Company entered into an amendment (the "Novartis Amendment") to the 2022 Novartis Agreement. Pursuant to the Novartis Amendment, the Company agreed to amend the 2022 Novartis Agreement to incorporate the grant to Novartis of a direct license (the "Novartis Direct License") to a TRACER Capsid (the "Novartis Direct Licensed Capsid") for exclusive use with a certain gene (the "Novartis Direct License Target") to develop and commercialize the Novartis Direct Licensed Capsid as incorporated into products containing a payload directed to the Novartis Direct License Target ("Novartis Direct Licensed Products"). (a) The two Initial Novartis Targets for which Novartis has exercised its Novartis License Options, and the Novartis Direct License Target collectively are the "Novartis Licensed Targets," and (b) the Novartis Initial Licensed Products and Novartis Direct Licensed Products collectively are "Novartis Licensed Products". As a result of the Novartis Amendment, the Novartis Direct License Target is now deemed a Novartis Licensed Target under the 2022 Novartis Agreement, as such term is defined therein, and the Novartis Direct License is subject to all other terms and conditions applicable to licenses granted to Novartis under the 2022 Novartis Agreement. In connection with the Novartis Amendment, the parties acknowledged that Novartis' prior rights to exercise options for any initial targets and additional targets as described in the 2022 Novartis Agreement, other than those that had previously been exercised, had expired as of the effective date of the Novartis Amendment.

During the period commencing on the Novartis Effective Date and ending on March 4, 2025 with respect to the Initial Novartis Targets and September 3, 2026 with respect to the Novartis Direct License Target (the Novartis Research Term"), on a target-by-target basis, the Company has granted Novartis a non-exclusive research license to evaluate the Company's TRACER Capsids for potential use, in combination with a payload directed the applicable Novartis Licensed Target. 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. Novartis may, during the applicable Novartis Research Term, conduct additional evaluation of the Company's capsid candidates and has the right to substitute any other TRACER Capsid for a Novartis Licensed Capsid.

Financial Terms

Under the terms of the 2022 Novartis Agreement, Novartis paid the Company an upfront payment of $54.0 million. In March 2023, Novartis exercised its Novartis License Options to license TRACER Capsids for use in gene therapy programs against two undisclosed Initial Novartis Targets. With Novartis' option exercise on two Initial Novartis Targets, the Company received a $25.0 million option exercise payment in April 2023. Novartis paid the Company a one-time fee of $15.0 million in consideration for the rights granted under the Novartis Amendment, which the Company received in October 2024. The Company is eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of $125.0 million for the first Novartis Initial Licensed Product for each Initial Novartis Target for which a Novartis License Option has been exercised to achieve the corresponding milestone. Additionally, the Company is eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of $130.0 million for the first Novartis Direct Licensed Product to achieve the corresponding milestone. On a Novartis Licensed Product-by-Novartis Licensed Product basis, the Company is also eligible to receive (a) specified sales milestone payments of up to an aggregate of $175.0 million per Novartis Licensed Product and (b) tiered, escalating royalties in the mid- to high-single-digit percentages based on annual net sales of each Novartis Licensed Product incorporating the Novartis Licensed Capsids.

Termination

Unless earlier terminated, the 2022 Novartis Agreement expires on the expiration of the last-to-expire royalty term with respect to all Novartis Licensed Products in all countries. Novartis may terminate the 2022 Novartis Agreement, in whole or in part, for any or no reason upon ninety days' written notice to the Company. The 2022 Novartis Agreement may also be terminated by either party under specific circumstances, including the other party's uncured material breach.

Upon certain terminations for cause by Novartis, the licenses granted by the Company to Novartis under the 2022 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 2022 Novartis Agreement was a contract with a customer under ASC 606. The Company assessed the promised goods and services and determined that the 2022 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 received a nonrefundable, upfront payment of $54.0 million as consideration under the 2022 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.

Novartis agreed to pay to the Company a one-time fee of $15.0 million in consideration for the rights granted under the Novartis Amendment, which was received in October 2024. The Company evaluated the Novartis Amendment under ASC 606 and recorded $15.0 million as collaboration revenue during the year ended December 31, 2024, since the consideration reflected the standalone selling price of the license that was delivered on the Novartis Amendment date, and there were no remaining undelivered performance obligations under the original 2022 Novartis Agreement. The Company is eligible to receive specified development, regulatory, and commercialization milestone payments of up to an aggregate of $130.0 million for the first Novartis Direct Licensed Product to achieve the corresponding milestone. On a Novartis Direct Licensed Product-by-Novartis Direct Licensed Product basis, the Company is also eligible to receive (a) specified sales milestone payments of up to an aggregate of $175.0 million per Novartis Direct Licensed Product and (b) tiered, escalating royalties in the mid- to high-single-digit percentages of annual net sales of each Novartis Direct Licensed Product.

During the year ended December 31, 2024, the Company recognized $15.0 million of collaboration revenue related to the Novartis Amendment from the one-time fee received in October 2024 discussed above. During the year ended December 31, 2023, the Company recognized $79.0 million in collaboration revenue related to the 2022 Novartis Agreement. Of this $79.0 million, $54.0 million was attributable to the exercise of the two material rights for Novartis License Options and the expiration of the third material right and was previously deferred as of December 31, 2022. The remaining $25.0 million represented the option exercise fee.

2023 Neurocrine Collaboration Agreement

Summary of Agreement

In January 2023, the Company entered into a collaboration and license agreement with Neurocrine (the "2023 Neurocrine Collaboration Agreement") for the research, development, manufacture and commercialization of gene therapy products designed to address Parkinson's disease and glucosylceramidase beta 1-mediated diseases (the "GBA1 Program"), and three early research programs focused on the research, development, manufacture and commercialization of gene therapies designed to address CNS-diseases or conditions associated with rare genetic targets (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 (the "Neurocrine Effective Date").

Collaboration and License

Under the 2023 Neurocrine Collaboration Agreement, the Company and Neurocrine have agreed to collaborate on the conduct of the 2023 Neurocrine Programs. Under the terms of the 2023 Neurocrine Collaboration Agreement, subject to the rights retained by the Company thereunder, the Company granted to Neurocrine, as of the Neurocrine Effective Date, an exclusive, royalty-bearing, sublicensable, worldwide license, under certain of the Company's intellectual property rights, to research, develop, manufacture and commercialize gene therapy products (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 the Company and Neurocrine (the "2023 Discovery Period"), and as overseen by the Joint Steering Committee for the ongoing collaboration with Neurocrine, the Company is responsible for identifying capsids meeting target criteria, producing development candidates, and conducting other pre-clinical activities regarding the 2023 Collaboration Products. With the exception of one preclinical study where the Company agreed to share costs, Neurocrine has agreed to be responsible for all costs the Company incurs in conducting pre-clinical development activities for each 2023 Neurocrine Program, in accordance with JSC agreed upon workplans and budgets. If the Company breaches its responsibilities during this time or, in certain circumstances, upon a change of control, Neurocrine has the right, but not the obligation, to assume the conduct of the Company's activities under such 2023 Neurocrine Program.

The Company has been granted the option ("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 the Company receiving topline data from the first Phase 1 clinical trial for a product candidate for Parkinson's disease being developed pursuant to the GBA1 Program. Should the Company elect to exercise its 2023 Co-Co Option, the Company and Neurocrine agree to enter into a cost and profit-sharing arrangement (a "2023 Co-Co Agreement"), whereby the Company and Neurocrine agree to jointly develop and commercialize 2023 Collaboration Products in the GBA1 Program ("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 the Company 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 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 the Company's 50% share of profits.

Candidate Selection

Either party may notify the JSC of any gene therapy product candidate that includes a Company capsid and a payload that is being developed under a 2023 Neurocrine Program (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 the Company 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 the Company conducts any portion of the manufacturing of a Collaboration Candidate, the applicable development plan shall include an obligation for the Company 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 the Company 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 the Company an upfront payment of approximately $136.0 million and approximately $39.0 million for the purchase of 4,395,588 shares of common stock of the Company at a price of $8.88 per share in February 2023. The 2023 Collaboration Agreement provides for aggregate development milestone payments from Neurocrine to the Company 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. 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 Company agreed to a forfeit certain milestones and royalties on net sales in the United States if the Company exercises the 2023 Co-Co Option. The JSC's selection of the development candidate for the GBA1 Program in April 2024 triggered a $3.0 million milestone payment, which the Company received in May 2024. Additionally, the JSC's selection of the development candidate for a 2023 Discovery Program in September 2024 triggered a $3.0 million milestone payment, which the Company received in October 2024.

Neurocrine has also agreed to pay the Company 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 (the "2023 Royalty Term"), subject to an anti-stacking provision. 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 each 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.

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. The 2023 Neurocrine Collaboration Agreement may also be terminated by either party under specific circumstances, including the other party's uncured material breach.

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 January 8, 2023 ("the "2023 Neurocrine Stock Purchase Agreement"), 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 2023 Neurocrine Stock Purchase Agreement, the Company issued and sold these shares to Neurocrine in February 2023.

Accounting Analysis

At inception, the Company determined the 2023 Neurocrine Collaboration Agreement was a contract with a customer under ASC 606 and that modification accounting was not required given that the 2023 Neurocrine Collaboration Agreement did not modify the scope or price of the 2019 Neurocrine Collaboration Agreement. The Company therefore determined that the 2023 Neurocrine Agreement should be accounted for separately. The 2023 Neurocrine Collaboration Agreement includes the following performance obligations: (i) the development and commercialization license for the GBA1 Program, (ii) the research and development services for the GBA1 Program, and (iii) the research and development services for each of the 2023 Discovery Programs combined with a development and commercialization license for each program. The license for the GBA1 Program is distinct as Neurocrine can benefit from such license on its own or from other resources commonly available in the industry given the stage of development of the product candidates subject to the license. Similarly, the research and development services for the GBA1 Program provide a distinct benefit to Neurocrine within the context of the contract, separate from the license. The research and development services for the 2023 Discovery Programs are not distinct as Neurocrine cannot benefit from such licenses 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 GBA1 license, GBA1 research and development services and the combined licenses and research and development services for the 2023 Discovery Programs are distinct from one another as Neurocrine can benefit from each program separately.

The Company identified $143.9 million of fixed transaction price consisting of the $136.0 million upfront fee, and a premium of $7.9 million related to the $39.0 million equity investment of 4,395,588 shares when measured at fair value on the date of issuance. The Company is also entitled to reimbursement of costs incurred by the Company during the 2023 Discovery Period associated with each of the GBA1 Program and 2023 Discovery Programs.

These amounts are determinable based on development plans, and the Company has a contractual right to the payment of costs incurred under the agreed upon program development plans.

The Company utilizes the most likely amount approach to estimate the cost reimbursement and has concluded this consideration should be constrained. As of December 31, 2024, the estimate of the expected reimbursement was $9.0 million of costs incurred based on expectations as of such date. The sales milestone payments and royalties will be recognized in the period the underlying sales occur, as this consideration is related to the two development and commercialization licenses, the predominant performance obligations in the contract.

The Company has allocated the fixed transaction price to the separate performance obligations based on the relative standalone selling price of each performance obligation. The estimated standalone selling prices for performance obligations were developed using the estimated selling price of the license for the GBA1 Program and each of the three 2023 Discovery Programs, using primarily adjusted market assessment approaches that considered discounted, probability-weighted cash flow analyses and entity-specific and market factors. The Company did not allocate any of the fixed transaction price to the GBA1 research and development services performance obligation as the consideration for such services reflects a market rate.

The Company concluded that the variable consideration related to the cost reimbursement of each program will be allocated to each respective program as the cost reimbursement relates specifically to the respective program services being performed under the 2023 Neurocrine Collaboration Agreement. The reimbursement of research services is at a market rate and the allocation of the fixed consideration to each of the three 2023 Discovery Program performance obligations depicts the estimated amounts in which it would expect to receive for these obligations, absent the variable consideration related to the research reimbursement. Based on the initial development plans, the total variable consideration allocated to each program related to the expected cost reimbursement was as follows as of December 31, 2024:

Performance Obligation	Amount
	(in thousands)
Variable Consideration	
GBA1 Program	$ 7,960
2023 Discovery Program 1	363
2023 Discovery Program 2	356
2023 Discovery Program 3	305
Total	$ 8,984

In April 2024, the JSC with Neurocrine selected a development candidate for the GBA1 program under the 2023 Neurocrine Collaboration Agreement. The JSC's selection of a development candidate for the GBA1 Program triggered a $3.0 million milestone payment to the Company. The Company recorded the $3.0 million as collaboration revenue during the second quarter of 2024.

In September 2024, the JSC with Neurocrine selected a development candidate in a gene therapy program for the potential treatment of an undisclosed neurological disease under the 2023 Neurocrine Collaboration Agreement, which triggered a $3.0 million milestone payment to the Company. The Company included the $3.0 million that had previously been constrained in the transaction price allocated to the program's performance obligation in the three months ended September 30, 2024, accordingly, which resulted in a cumulative catch-up adjustment to collaboration revenue of approximately $2.0 million.

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

Performance Obligation	Amount
	(in thousands)
Fixed Consideration	
GBA1 Program	$ 72,459
2023 Discovery Program 1	27,807
2023 Discovery Program 2	24,807
2023 Discovery Program 3	24,807
Total	$ 149,880

The Company recognized the fixed transaction price allocated to the development and commercialization license for the GBA1 Program as collaboration revenue in the first quarter of 2023, upon delivery of the development and commercialization license for the GBA1 Program to Neurocrine. The Company is recognizing the consideration allocated to each of the three 2023 Discovery Program performance obligations on a proportional performance basis over the period of service using input-based measurements such as costs incurred to date, to estimate proportion performed, and remeasures its progress towards completion at the end of each reporting period. Proportional performance is determined based on the workplan cost and timeline estimates.

During the year ended December 31, 2024, the Company recognized $44.5 million of collaboration revenue associated with the fixed transaction price allocated to the three 2023 Discovery Programs, $3.0 million of collaboration

revenue associated with the selection of a development candidate for the GBA1 Program, and $2.2 million of collaboration revenue associated with research and development services performed during the period and the corresponding cost reimbursement receivable. As of December 31, 2024, there was $27.6 million of deferred revenue related to the 2023 Neurocrine Collaboration Agreement, of which $22.3 million was classified as current and $5.3 million was classified as non-current in the accompanying balance sheets based on the period the services are expected to be delivered. Additionally, as of December 31, 2024, there was $0.3 million of related party collaboration receivable related to reimbursable costs expected to be received from Neurocrine for research and development services performed.

During the year ended December 31, 2023, the Company recognized $69.5 million of revenue associated with the 2023 Neurocrine Collaboration Agreement related to the delivery of the development and commercialization license for the GBA1 Program. During the year ended December 31, 2023, the Company recognized $5.8 million of collaboration revenue associated with research and development services performed during the period and the corresponding cost reimbursement receivable for the GBA1 Program. During the year ended December 31, 2023, the Company recognized a total of $5.5 million of revenue associated with the fixed transaction price allocated to the three 2023 Discovery Programs, and for research and development services performed during the period. As of December 31, 2023, there was $69.1 million of deferred revenue related to the 2023 Neurocrine Collaboration Agreement, of which $38.4 million was classified as current and $30.7 million was classified as non-current in the accompanying balance sheets based on the period the services are expected to be delivered. Additionally, as of December 31, 2023, there was $1.8 million of related party collaboration receivable related to reimbursable costs expected to be received from Neurocrine for research and development services performed.

The Company incurred approximately $0.4 million of costs to obtain the 2023 Neurocrine Collaboration Agreement which were payable only upon the close of the transaction and therefore considered incremental costs of obtaining a contract with a customer and capitalized. The costs are recorded in prepaid expenses and are being amortized to operating expenses consistent with the manner in which the consideration allocated to the performance obligations is recognized.

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) a program for the treatment of Friedreich's ataxia (the "FA Program" and, 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 Corporation, 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 and the Company is no longer eligible to receive milestone or royalty payments related to the VY-AADC Program.

Collaboration and License

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 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 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 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 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.

Candidate Selection

Under the 2019 Neurocrine Collaboration Agreement, the parties committed to agree on a list of up to eight target genes 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 approved the two targets for development under the 2019 Discovery Programs. The two targets are currently under development.

Financial Terms

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 FA Program of up to $195.0 million, and (b) 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. The JSC's selection of the development candidate for the FA Program in February 2024 triggered a $5.0 million milestone payment, which the Company received in March 2024. 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 FA Program, from the low-teens to high-teens and high-single digits to mid-teens, respectively; and (b) 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. 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.

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 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 2019 Neurocrine Collaboration Agreement may also be terminated by either party under specific circumstances, including the other party's uncured material breach.

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. During the fourth quarter of 2023, the Company further revised the estimate of the expected reimbursement to approximately $83.3 million, based on expectations resulting from decisions made at the JSC meeting held in the fourth quarter of 2023. 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 as of December 31, 2024, was as follows:

Performance Obligation	**Amount**
	(in thousands)
Variable Consideration	
VY-AADC Program	$ 53,863
FA Program	19,560
2019 Discovery Program 1	4,546
2019 Discovery Program 2	4,401
Total	$ 82,370

In February 2024, the JSC with Neurocrine selected a lead development candidate for the FA Program under the 2019 Neurocrine Collaboration Agreement, which triggered a $5.0 million milestone payment to the Company that was received in the first quarter of 2024. The Company included the $5.0 million that had previously been constrained in the transaction price allocated to the FA Program performance obligation in the three months ended March 31, 2024, accordingly, which resulted in a cumulative catch-up adjustment to collaboration revenue of $4.4 million.

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	25,647
2019 Discovery Program 1	14,443
2019 Discovery Program 2	8,247
Total	$ 97,382

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

During the year ended December 31, 2024 and 2023, the Company recognized $10.4 million and $9.8 million of revenue, respectively, associated with its collaboration with Neurocrine related to fixed transaction price allocated to the three active programs, and research and development services performed during the period and the corresponding cost reimbursement receivable. As of December 31, 2024, there was $2.8 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, 2024, there was $0.4 million of collaboration receivable 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 receivable and contract liabilities for both the 2023 Neurocrine Collaboration Agreement and the 2019 Neurocrine Collaboration Agreement during the year ended December 31, 2024:

	Balance at December 31, 2023	Additions	Deductions	Balance at December 31, 2024
		(in thousands)		
Related party collaboration receivables	$ 3,341	$ 12,269	$ (14,934)	$ 676
Contract liabilities:				
Deferred revenue	$ 75,240	$ 1,592	$ (46,435)	$ 30,397

The change in the related party collaboration receivable balance for the year ended December 31, 2024 is primarily driven by amounts owed to the Company for research and development services provided, offset by amounts collected from Neurocrine during the period, for both the 2023 Neurocrine Collaboration Agreement and the 2019 Neurocrine Collaboration Agreement. Deferred revenue activity for the year ended December 31, 2024 includes the recording of $1.6 million of deferred revenue during the year ended December 31, 2024 related to fixed transaction price allocation increases, offset by $46.4 million of collaboration revenue recognized on the proportional performance model during the year ended December 31, 2024 for both the 2023 Neurocrine Collaboration Agreement and 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.

Alexion Option and License Agreement (Formerly Pfizer Option and License Agreement)

Summary of Agreement

The Company is party to an option and license agreement with Alexion (the "Alexion Agreement"). The Company initially entered into the Alexion Agreement with Pfizer, Inc. ("Pfizer") in October 2021 (the "Alexion Agreement Effective Date"). However, Alexion (via Alexion Pharma International Operations Limited ("APIO")) later acquired all of Pfizer's rights under the Alexion Agreement and became the successor-in-interest to Pfizer thereunder effective upon the closing of a definitive purchase and license agreement between Pfizer and Alexion in September 2023. APIO subsequently assigned the Alexion Agreement to its affiliate AstraZeneca Ireland Limited ("AstraZeneca"). Neither the acquisition by Alexion nor the subsequent assignment from APIO to AstraZeneca impacted the material terms of the Alexion Agreement. Pursuant to the Alexion Agreement, the Company has granted Alexion an exclusive, worldwide license, with the right to sublicense, under certain of its intellectual property, the rights to develop and commercialize AAV gene therapy products for the potential treatment of a rare neurological disease comprised of a TRACER Capsid (the "Alexion Licensed Capsid"), and a specified transgene (the "Alexion Transgene"). Such AAV gene therapy products are referred to as "Alexion Licensed CNS Products."

Prior to Alexion's acquisition of all of Pfizer's rights under the Alexion Agreement, we had granted Pfizer the right to exercise up to two options to license TRACER Capsids to develop and commercialize certain AAV gene therapy candidates comprised of a TRACER capsid and a specified transgene. In September 2022, Pfizer exercised its option with respect to a TRACER Capsid for a specified transgene for potential treatment of a rare neurological disease. All of Pfizer's rights in connection with such option exercise were transferred to Alexion as discussed above. Pfizer did not exercise its option with respect to any TRACER Capsid for a specified transgene for the potential treatment of a cardiovascular disease. As result, all rights to any TRACER Capsids for that cardiovascular disease reverted to the Company in accordance with the terms of the Alexion Agreement.

Financial Terms

Prior to Pfizer's transfer of its rights under of the Alexion Agreement, Pfizer paid the Company an upfront payment of $30.0 million in October 2021, and an additional fee of $10.0 million in connection with its exercise of an option. 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 Alexion Licensed CNS Product to achieve the corresponding milestone. On an Alexion Licensed CNS Product-by-Alexion 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 Alexion Licensed CNS Product and (b) tiered, escalating royalties in the mid- to high-single-digit percentages of annual net sales of each Alexion 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 Alexion Agreement expires on the expiration of the last-to-expire royalty term with respect to all Alexion Licensed CNS Products in all countries. Alexion may also terminate the Alexion Agreement, in whole or in part, for any or no reason upon ninety days' written notice to the Company. The Alexion Agreement may also be terminated by either party under specific circumstances, including the other party's uncured material breach.

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

Accounting Analysis

At inception, the Company determined the Alexion Agreement was a contract with a customer under ASC 606. The Company assessed the promised goods and services under the Alexion Agreement, in accordance with ASC 606,

and determined that the Alexion Agreement contains two performance obligations consisting of two material rights, one for each of the options to license a TRACER Capsid.

The Company received a nonrefundable, upfront payment of $30.0 million as consideration under the Alexion Agreement, which represented the transaction price at inception.

The Company allocated the transaction price to the options based on their relative standalone selling prices, or $15.0 million for each material right.

During the year ended December 31, 2022, the Company recognized $40.0 million in collaboration revenue related to the Alexion Agreement. No revenue was recognized under the Alexion Agreement for the years ended December 31, 2024, and December 31, 2023.

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 included a one-time, non-refundable technology access fee of $5.0 million, which was expensed as research and development expense in the year ended December 31, 2022.

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.

During the year ended December 31, 2023, the Company recorded $0.5 million in research and development expense associated with amounts due to Touchlight in conjunction with the 2023 Novartis Collaboration Agreement. During the year ended December 31, 2024, no research and development expense was recognized under the license agreement with Touchlight.

10. Common stock

As of December 31, 2024, and 2023, the Company had authorized 120,000,000 shares of common stock, at $0.001 par value per share.

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 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,	
	2024	2023
Shares reserved for vesting of restricted stock awards under the Founder Agreements	—	22,500
Shares reserved for exercise of outstanding stock options	8,800,464	7,425,444
Shares reserved for vesting of outstanding restricted stock units	1,649,943	1,370,897
Shares reserved for issuances under the 2015 Stock Option Plan	3,765,132	3,572,195
Shares reserved for issuances under the 2015 Employee Stock Purchase Plan	2,010,897	2,158,966
	16,226,436	14,550,002

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.

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 Company's initial public offering ("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 14,717,369 shares through January 1, 2025. During the year ended December 31, 2024, the Company granted options to purchase 1,921,326 shares of common stock to employees and directors under the 2015 Stock Option Plan. As of December 31, 2024, there were 3,765,132 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.

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 3,132,873 shares through January 1, 2025. The Company issued 148,069 and 111,639 shares of common stock under the 2015 ESPP in the years ended December 31, 2024, and 2023. As of December 31, 2024, there were 2,010,897 shares available for future purchase under the 2015 ESPP.

Inducement Awards

In the years ended December 31, 2024, 2023 and, 2022, the Company issued non-statutory stock options to purchase an aggregate of 486,000, 573,000, and 390,000 shares of the Company's common stock and restricted stock unit awards for an aggregate of 223,000, 318,500, and 163,000 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,		
	2024	2023	2022
	(in thousands)		
General and administrative	$ 8,746	$ 7,568	$ 6,398
Research and development	6,039	3,585	2,946
Total stock-based compensation expense	$ 14,785	$ 11,153	$ 9,344

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,		
	2024	2023	2022
		(in thousands)	
Stock options	$ 9,727	$ 7,627	$ 5,938
Restricted stock awards and units	4,734	3,241	3,215
Employee stock purchase plan awards	323	285	191
Total stock-based compensation expense	$ 14,785	$ 11,153	$ 9,344

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, 2024, was as follows:

	Units	Weighted Average Grant Date Fair Value Per Unit
Unvested restricted stock units as of December 31, 2023	1,370,897	$ 6.65
Awarded	1,010,208	$ 7.83
Vested	(515,303)	$ 6.42
Forfeited	(215,859)	$ 6.67
Unvested restricted stock units as of December 31, 2024	1,649,943	$ 7.44

Stock-based compensation of restricted stock units is based on the fair value of the Company's common stock on the date of grant and is recognized over the vesting period. In the year ended December 31, 2024, the Company granted 1,010,208 restricted stock units vesting in equal amounts, annually over three years.

As of December 31, 2024, the Company had unrecognized stock-based compensation expense related to its unvested restricted stock units of $8.6 million which is expected to be recognized over the remaining weighted average vesting period of 1.5 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, 2023	7,425,444	$ 8.52		
Granted	2,407,326	$ 7.75		
Exercised	(106,831)	$ 4.49		
Cancelled or forfeited	(925,475)	$ 10.98		
Outstanding at December 31, 2024	8,800,464	$ 8.10	7.3	3,462
Exercisable at December 31, 2024	4,837,929	$ 8.45	6.4	$ 2,732

Using the Black-Scholes option pricing model, the weighted average fair value of options granted during the years ended December 31, 2024, 2023, and 2022, was $5.45, $6.12, and $3.60, 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,		
	2024	2023	2022
Risk-free interest rate	4.1 %	4.0 %	2.2 %
Expected dividend yield	— %	— %	— %
Expected term (in years)	6.0	6.0	6.0
Expected volatility	76.3 %	80.4 %	79.4 %

As of December 31, 2024, the Company had unrecognized stock-based compensation expense related to its unvested stock options of $18.0 million which is expected to be recognized over the remaining weighted average vesting period of 2.8 years.

12. Underwritten public offering

In January 2024, the Company entered into an underwriting agreement relating to an underwritten public offering of 7,777,778 shares of the Company's common stock, par value $0.001 per share, and, in lieu of common stock to certain investors, pre-funded warrants (the "Pre-Funded Warrants") to purchase up to 3,333,333 shares of common stock. The underwriters agreed to purchase the Company's stock at a price of $8.46 and the Pre-Funded Warrants at a price of $8.459 per share underlying each Pre-Funded Warrant. The Company issued 7,777,778 shares of common stock and 3,333,333 Pre-Funded Warrants for net proceeds of approximately $93.5 million after deducting underwriting discounts and commissions and offering expenses pursuant to the underwritten public offering. The Pre-Funded Warrants met the equity classification guidance and therefore are classified as stockholders' equity.

13. 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 $1.4 million, $1.1 million, and $0.9 million related to employer contributions made during the years ended December 31, 2024, 2023, and 2022, respectively.

14. Income taxes

The provision for incomes taxes is as follows:

	Year ended December 31,		
	2024	2023	2022
	(in thousands)		
Current			
Federal	$ 443	$ 1,248	$ —
State	222	160	16
Total current	665	1,408	16
Deferred			
Federal	—	—	—
State	—	—	—
Total deferred	—	—	—
Total tax provision	$ 665	$ 1,408	$ 16

A reconciliation of the expected income tax provision computed using the federal statutory income tax rate at the Company's effective tax rate is as follows:

	Year ended December 31,		
	2024	2023	2022
Income tax computed at federal statutory tax rate	21.0 %	21.0 %	21.0 %
State taxes, net of federal benefit	9.3 %	5.4 %	5.2 %
General business credits	8.3 %	(0.4)%	(3.5)%
Provision to return	0.1 %	0.9 %	3.2 %
Non-deductible expenses	(1.1)%	0.5 %	(4.6)%
Other	(3.4)%	(0.4)%	— %
Change in valuation allowance	(35.0)%	(26.0)%	(21.3)%
Total	(0.8)%	1.00 %	— %

The Company has historically incurred net operating losses ("NOLs"). As of December 31, 2024, the Company had federal and state net operating loss carryforwards of $20.0 million and $0.8 million, respectively. As of December 31, 2024, the Company had federal and state research and development tax credit carryforwards of $23.6 million and $13.73 million, respectively, which expire beginning in 2033. As of December 31, 2024, the Company had $0.4 million of state investment credits.

The significant components of the Company's deferred tax assets and (liabilities) are as follows:

	As of December 31,	
	2024	2023
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforward	$ 4,244	$ 13,724
Tax credit carryforwards	34,424	28,427
Lease liability	11,946	5,544
Deferred revenue	7,867	1,675
Stock-based compensation	5,328	5,157
Non-deductible accruals and reserves	2,435	2,613
Capitalized research expenses	50,974	31,347
Intangibles	499	554
Total deferred tax assets	117,717	89,041
Less valuation allowance	(105,854)	(82,612)
Net deferred tax assets	11,863	6,429
Deferred tax liabilities		
Right of use assets	(9,111)	(3,691)
Depreciation and amortization	(2,752)	(2,738)
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, tax credit carryforwards, and capitalized research expenses. 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 $105.9 million and $82.6 million has been established at December 31, 2024 and 2023, respectively. The state NOLs will expire beginning in 2041 while the federal NOLs do not expire. The valuation allowance decreased by $23.3 million for the year ended December 31, 2024. 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, 2024 and 2023, the Company had no unrecognized tax benefits. The Company completed a study of its research and development credit carryforwards in 2024. The Company has recorded an adjustment in the current year to reflect the preliminary results of the research and development study. The completion of the study may result in an additional adjustment to the Company's research and development credit carryforwards; however, until a study is completed, 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 and comprehensive (loss) income if an adjustment were required.

Sections 382 and 383 of the U.S. Internal Revenue Code ("IRC") impose substantial restrictions on the utilization of net operating losses and other tax attributes in the event of a cumulative "ownership change". In general, a company would undergo an ownership change if its "5-percent shareholders" (determined under Section 382) increased their collective ownership of the company's stock by more than 50% over a rolling three-year period. Accordingly, if the Company generates taxable income in the future, changes in our stock ownership, including equity offerings and share repurchase programs, as well as other changes that may be outside its control, could potentially result in material limitations on the Company's ability to use its net operating loss and research tax credit carryforwards. Similar rules may

apply under state tax laws. The Company has not conducted a Section 382 or Section 383 study to determine whether the use of its net operating losses and research tax credits is limited. The Company may have experienced ownership changes in the past, and it may experience ownership changes in the future, some of which are outside of its control. This could limit the amount of net operating losses and research tax credits that the Company can utilize annually to offset future taxable income or tax liabilities. Subsequent statutory or regulatory changes in respect to the utilization of net operating losses and research tax credits for federal or state purposes, such as suspensions or limitations on the use of net operating losses and research tax credits carried forward, or other unforeseen reasons, may result in the Company's existing net operating losses and research tax credits expiring or otherwise being unavailable to offset future income tax liabilities.

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, 2024, and 2023, 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.

15. Related-party transactions

During the years ended December 31, 2024, 2023, and 2022, the Company received scientific advisory services from one of its prior executives, Dinah Sah, Ph.D., the Company's former Chief Scientific Officer. The total amount of fees paid to Dr. Sah for services provided during the years ended December 31, 2024, 2023 and 2022 was $0.7 million, $0.7 million, and $0.5 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 both the 2019 Neurocrine Collaboration Agreement and the 2023 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 receivable. As of December 31, 2024, the Company recorded approximately $0.7 million in related party collaboration receivable relative to the 2019 Neurocrine Collaboration Agreement and the 2023 Neurocrine Collaboration Agreement. As of December 31, 2023, the Company recorded approximately $3.3 million in related party collaboration receivable relative to the 2019 Neurocrine Collaboration Agreement and the 2023 Neurocrine Collaboration Agreement.

16. Segment Information

The Company's CODM, the Company's Chief Executive Officer, views the Company's operations and manages its business as a single operating segment, which is the business of developing and commercializing genetic medicine. The Company therefore has one reportable segment.

The CODM reviews the segment's profit or loss based on net (loss) income reported on the consolidated statement of operations and comprehensive (loss) income and considers forecast-to-actual variances monthly for expenses that are deemed significant in making resource allocation decisions and assessing performance. Further, the CODM reviews the segment's assets based on total assets reported on the consolidated balance sheets. All long-lived assets are held in the United States.

The CODM views specific categories within research and development expenses and general and administrative expenses in totality as significant. Further, the CODM reviews the external research and development expenses of specific programs as significant given the impact on achieving the Company's corporate goals. The following table

reconciles reported collaboration revenue to net (loss) income under the significant expense principle for the years ended December 31, 2024, 2023, and 2022:

	Year ended December 31, 2024	Year ended December 31, 2023	Year ended December 31, 2022
Collaboration revenue	$ 80,001	$ 250,008	$ 40,907
External research and development (1):			
Anti-tau antibody program	15,647	16,923	1,190
SOD1 silencing gene therapy program	15,818	6,251	3,082
Tau silencing gene therapy program	7,455	696	—
Partnered programs (2)	4,985	7,650	3,229
Other programs and platforms (3)	14,176	14,488	14,721
Internal research and development (4)	38,422	27,860	20,505
Facilities and other research and development (5)	30,865	18,304	18,037
General and administrative	35,920	35,822	30,980
Interest income	18,328	11,721	1,792
Other income	622	3	2,653
Income tax provision	665	1,408	16
Net (loss) income	$ (65,002)	$ 132,330	$ (46,408)

1) External research and development is allocated to the Company's programs and platforms, and includes laboratory supplies, and non-employee consultant and contractor costs.
2) Partnered programs include programs in which the Company is collaborating with partners to develop AAV gene therapy products and product candidates under the Company's 2019 and 2023 Neurocrine Collaboration Agreements, and the 2023 Novartis Collaboration Agreement.
3) Other programs and platforms consist of expenses related to other early research programs and platforms which are not considered quantitatively and qualitatively significant, including capsid discovery, non-viral delivery, and early research programs.
4) Internal research and development consist of employee-related expenses including salaries, benefits, and stock-based compensation expense.
5) Depreciation and amortization are included within facilities and other research and development, which are the same as the amounts in the accompanying consolidated statements of operations as the Company operates as a single operating segment.

EXHIBIT INDEX

		Incorporated by Reference to:				
Exhibit No.	Description	Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number	Filed Herewith
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	
4.2	Form of Pre-Funded Warrant	8-K	4.1	01/08/2024	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 64 Sidney Street, LLC, dated December 23, 2015	10-Q	10.6	05/12/2016	001-37625
10.11	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
10.12	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
10.13	Form of Indemnification Agreement to be entered into between the Registrant and its directors	S-1/A	10.9	10/28/2015	333-207367

10.14	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
10.15#	2015 Employee Stock Purchase Plan	S-1/A	10.12	10/28/2015	333-207367
10.16#	Amendment No. 1 to the 2015 Employee Stock Purchase Plan	10-K	10.21	03/14/2018	001-37625
10.17#	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
10.18#	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
10.19#	Form of Non-Qualified Stock Option Agreement for Inducement	10-K	10.27	02/26/2019	001-37625
10.20#	Form of Restricted Stock Unit Agreement for Inducement	10-K	10.33	02/26/2019	001-37625
10.21	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
10.22*	Option and License Agreement by and between the Registrant and Novartis Pharma AG, dated March 4, 2022	10-K	10.36	03/07/2023	001-37625
10.23#	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

10.24#	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
10.25*	Patent and Know-How License between the Registrant and Touchlight IP Limited, dated as of November 3, 2022.	10-K	10.43	03/07/2023	001-37625
10.26	Stock Purchase Agreement by and between the Registrant and Neurocrine Biosciences, Inc., dated as of January 8, 2023.	10-K	10.44	03/07/2023	001-37625
10.27*	Collaboration and License Agreement by and between the Registrant and Neurocrine Biosciences, Inc., dated as of January 8, 2023.	10-K	10.45	03/07/2023	001-37625
10.28	Amended and Restated Investor Agreement by and between the Registrant and Neurocrine Biosciences, Inc., dated as of January 8, 2023.	10-K	10.46	03/07/2023	001-37625
10.29#	Employment Agreement by and between the Registrant and Jacquelyn Fahey Sandell, effective as of July 5, 2023.	8-K	10.1	07/10/2023	001-37625
10.30	First Amendment to Lease Agreement, by and between Registrant and LS 75 Hayden, LLC, dated August 11, 2023.	8-K	10.1	08/16/2023	001-37625
10.31*	License and Collaboration Agreement by and between Registrant and Novartis Pharma AG, dated December 28, 2023.	10-K	10.43	02/28/2024	001-37625

10.32	Stock Purchase Agreement by and between Registrant and Novartis Pharma AG, dated December 28, 2023.	10-K	10.44		02/28/2024	001-37625
10.33	Investor Agreement by and between Registrant and Novartis Pharma AG, dated December 28, 2023.	10-K	10.45		02/28/2024	001-37625
10.34#	Employment Agreement, by and between the Registrant and Toby Ferguson, M.D., Ph.D., dated as of February 29, 2024.	8-K	10.1	03/13/2024		001-37625
10.35#	Transition, Separation and Release of Claims Agreement, by and between the Registrant and Peter P. Pfreundschuh, dated April 1, 2024.	8-K	10.1	04/02/2024		001-37625
10.36#	Consulting Agreement by and between the Registrant and Peter P. Pfreundschuh, dated as of May 6, 2024.	10-Q	10.4	05/13/2024		001-37625
10.37*	First Amendment to Collaboration and License Agreement, by and between Registrant and Neurocrine Biosciences, Inc., dated April 3, 2024.	10-Q	10.1	08/06/2024		001-37625
10.38	Employment Agreement, by and between the Registrant and Nathan Jorgensen, Ph.D., dated as of July 8, 2024.	8-K	10.1	06/13/2024		001-37625
10.39*	First Amendment to Option and License Agreement, by and between Registrant and Novartis Pharma AG, dated September 3, 2024.	10-Q	10.1	11/12/2024		001-37625

10.40*	First Amendment to Option and License Agreement, by and between Registrant and AstraZeneca Ireland Limited, dated September 30, 2024.	10-Q	10.2	11/12/2024	001-37625		
19.1	Amended and Restated Insider Trading Policy						X
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	
97.1	Compensation Recovery Policy	10-K	97.1	02/28/2024	001-37625		
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.

Date: March 11, 2025

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 Nate Jorgensen, 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 11, 2025
/s/ Nathan Jorgensen, Ph.D. Nathan Jorgensen, Ph.D.	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 11, 2025
/s/ Michael Higgins Michael Higgins	Director (Chairman of the Board)	March 11, 2025
/s/ Grace E. Colón, Ph.D. Grace E. Colón, Ph.D.	Director	March 11, 2025
/s/ James Geraghty James Geraghty	Director	March 11, 2025
/s/ Steven Hyman, M.D. Steven Hyman, M.D.	Director	March 11, 2025
/s/ Catherine J. Mackey, Ph.D. Catherine J. Mackey, Ph.D.	Director	March 11, 2025
/s/ Jude Onyia, Ph.D. Jude Onyia, Ph.D.	Director	March 11, 2025
/s/ Glenn Pierce, M.D., Ph.D. Glenn Pierce, M.D., Ph.D.	Director	March 11, 2025
/s/ George Scangos, Ph.D. George Scangos, Ph.D.	Director	March 11, 2025
/s/ Nancy Vitale Nancy Vitale	Director	March 11, 2025

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LEADERSHIP TEAM

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

Todd Carter
Chief Scientific Officer

Jacquelyn Fahey Sandell, J.D.
Chief Legal Officer

Toby Ferguson, M.D., Ph.D.
Chief Medical Officer

Nathan Jorgensen, Ph.D.
Chief Financial Officer

Trista Morrison
Chief Corporate Affairs Officer and Chief of Staff to the CEO

Michelle Quinn Smith
Chief Human Resources Officer

Robin Swartz
Chief Business Officer and Chief Operating Officer

BOARD OF DIRECTORS

Michael Higgins *(Chair)*

Chairman of the Board of Directors: Pulmatrix, Inc.; Nocion Therapeutics, Inc.

Board Member: Cyclerion Therapeutics, Inc.; Camp4 Therapeutics Corporation; Sea Pharmaceuticals, LLC

Grace E. Colón, Ph.D.

Chair of the Board of Directors: Bloom Science, Inc.; Emm Technology Ltd.

Board Member: Inaya Therapeutics, Inc.; Massachusetts Institute of Technology (MIT) Corp. *(term member)*; Biotechnology Innovation Organization

James A. Geraghty

Chairman of the Board of Directors: CANbridge Pharmaceuticals Inc.

Board Member: Fulcrum Therapeutics, Inc.; OMass Therapeutics

Steven Hyman, M.D.

Board Member: Cyclerion Therapeutics, Inc.; Program in Brain Health 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: IDEAYA Biosciences, Inc.

Jude Onyia, Ph.D.

Chief Scientific Officer, Neurocrine Biosciences, Inc.

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

Board Member: World Federation of Hemophilia

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

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

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

George Scangos, Ph.D.

Board Member: Agilent Technologies, Inc.; Vir Biotechnology, Inc.; Life Science Cares; Octave Bioscience, Inc.; Rezo Therapeutics,Inc.

Nancy Vitale

Chief People Officer, Omada Health, Inc.

voyager therapeutics

Voyager Therapeutics, Inc.
75 Hayden Avenue
Lexington, MA 02421

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 3, 2025, 11:00 am ET